Supporting Information

Enantioselective Total Synthesis of (+)-Azimine and (+)-Carpaine

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(4E,6Z/E)-7-[(2S,4S)-2-Phenyl-1,3-dioxan-4-yl]hepta-4,6-dien-1-ol (12). (4E,6Z)-isomer/(4E,6E)-isomer = 6:1. IR (neat) 3417, 1655 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) the (4E,6Z)-isomer δ 1.53 (d, $J = 13.6$ Hz, 1H), 1.62 (quint, $J = 7.0$ Hz, 2H), 1.96 (qd, $J = 12.4$, 4.8 Hz, 1H), 2.18 (q, $J = 7.3$ Hz, 2H), 3.55 (t, $J = 6.4$ Hz, 2H), 4.02 (td, $J = 12.0$, 2.1 Hz, 1H), 4.27 (dd, $J = 11.3$, 4.6 Hz, 1H), 4.81 (br td, $J = 8.8$, 1.6 Hz, 1H), 5.41 (dd, $J = 10.9$, 8.1 Hz, 1H), 5.60 (s, 1H), 5.76 (dt, $J = 15.0$, 7.0 Hz, 1H), 6.06 (t, $J = 11.1$ Hz, 1H), 6.39 (ddd, $J = 14.9$, 11.2, 1.0 Hz, 1H), 7.31–7.39 (m, 3H), 7.49–7.54 (m, 2H); ^{13}C NMR (100.6 MHz, CDCl_3) δ 28.9, 31.3, 31.8, 61.8, 66.7, 73.7, 101.0, 125.5, 126.0 (2 carbons), 128.0 (2 carbons), 128.1, 128.6, 130.4, 136.6, 138.4; HRMS (ESI–TOF) m/z Calcd for $\text{C}_{17}\text{H}_{22}\text{O}_3\text{Na}$ $[\text{M} + \text{Na}]^+$ 297.1467, found 297.1493.

(3S,4Z/E,6E)-3-(Benzyloxy)-10-(methoxymethoxy)deca-4,6-dien-1-ol (13). (4E,6Z)-isomer/(4E,6E)-isomer = 6:1. IR (neat) 3442, 1653 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) the (4E,6Z)-isomer δ 1.61–1.79 (m, 3H), 1.84–1.96 (m, 1H), 2.19 (q, $J = 7.3$ Hz, 2H), 2.56 (br s, 1H), 3.35 (s, 3H), 3.53 (t, $J = 6.5$ Hz, 2H), 3.67–3.81 (m, 2H), 4.33 and 4.59 (ABq, $J = 11.8$ Hz, 2H), 4.50 (td, $J = 8.84$, 4.7 Hz, 1H), 4.61 (s, 2H), 5.29 (t, $J = 9.9$ Hz, 1H), 5.76 (dt, $J = 14.4$, 7.0 Hz, 1H), 6.13–6.30 (m, 2H), 7.24–7.36 (m, 5H); ^{13}C NMR (100.6 MHz, CDCl_3) δ 29.2, 29.4, 37.9, 55.1, 60.5, 67.0, 70.1, 73.7, 96.4, 125.5, 127.6, 127.9 (2 carbons), 128.4 (2 carbons), 129.1, 131.9, 136.5, 138.3; HRMS (ESI–TOF) m/z Calcd for $\text{C}_{19}\text{H}_{28}\text{O}_4\text{Na}$ $[\text{M} + \text{Na}]^+$ 343.1885, found 343.1905.

(3S,4E,6E)-3-(Benzyloxy)-10-(methoxymethoxy)deca-4,6-dienyl 4-Methylbenzenesulfonate (14): $[\alpha]_{\text{D}}^{23} +0.083$ (c 1.20, CHCl_3); IR (neat) 1653 cm^{-1} ; ^1H NMR (400 MHz,

CDCl₃) δ 1.71 (quint, J = 7.0 Hz, 2H), 1.80–1.98 (m, 2H), 2.20 (q, J = 7.3 Hz, 2H), 2.41 (s, 3H), 3.37 (s, 3H), 3.54 (t, J = 6.5 Hz, 2H), 3.88 (td, J = 8.1, 4.9 Hz, 1H), 4.05–4.14 (m, 1H), 4.19–4.25 (m, 1H), 4.20 and 4.50 (ABq, J = 11.4 Hz, 2H), 4.62 (s, 2H), 5.39 (dd, J = 14.9, 8.2 Hz, 1H), 5.72 (dt, J = 14.7, 7.2 Hz, 1H), 6.08–6.23 (m, 2H), 7.19–7.24 (m, 2H), 7.27–7.34 (m, 5H), 7.74–7.80 (m, 2H); ¹³C NMR (100.6 MHz, CDCl₃) δ 21.6, 29.2, 29.3, 35.2, 55.2, 67.1, 67.3, 70.2, 75.8, 96.5, 127.5, 127.7 (2 carbons), 127.9 (2 carbons), 128.3 (2 carbons), 129.6, 129.8 (2 carbons), 130.2, 133.1, 133.7, 135.2, 138.3, 144.7; HRMS (ESI-TOF) m/z Calcd for C₂₆H₃₄O₆SNa [M + Na]⁺ 497.1974, found 497.2004.

(4*S*,5*E*,7*E*)-4-(Benzyloxy)-*N*-hydroxy-11-(methoxymethoxy)undeca-5,7-dienamide (15): [α]_D²² –26.3 (c 0.75, CHCl₃); IR (neat) 3241, 1658 cm^{–1}; ¹H NMR (400 MHz, CDCl₃) δ 1.70 (br t, J = 6.6 Hz, 2H), 1.86 (br d, J = 6.1 Hz, 2H), 2.10–2.23 (m, 4H), 3.36 (m, 3H), 3.53 (t, J = 6.4 Hz, 2H), 3.72–3.88 (m, 1H), 4.28 and 4.55 (ABq, J = 11.7 Hz, 2H), 4.60 (s, 2H), 5.43 (dd, J = 15.1, 8.0 Hz, 1H), 5.65–5.80 (m, 1H), 6.05 (dd, J = 14.8, 11.4 Hz, 1H), 6.17 (dd, J = 14.8, 10.5 Hz, 1H), 7.25–7.36 (m, 5H), 8.70–9.30 (br s, 1H); ¹³C NMR (100.6 MHz, CDCl₃) δ 29.1, 29.2, 29.3, 31.1, 55.1, 67.1, 70.1, 78.7, 96.4, 127.7, 127.9 (2 carbons), 128.4 (2 carbons), 129.7, 130.4, 133.4, 135.0, 138.3, 171.2; HRMS (ESI-TOF) m/z Calcd for C₂₀H₂₉NO₅Na [M + Na]⁺ 386.1943, found 386.1940.

Intramolecular Acylnitroso-Diels–Alder Reaction. To an ice-cooled, vigorously stirred solution of NaIO₄ (118 mg, 0.552 mmol) in water (100 mL) was added a solution of **15** (100 mg, 0.275 mmol) in DMF (2 mL) by portions. After being stirred at 0 °C for 15 min, the reaction mixture was quenched by addition of solid Na₂S₂O₃·5H₂O (200 mg, 0.806 mmol). The mixture was extracted with CHCl₃ (3 x 150 mL) and the combined extracts were washed with water and dried (MgSO₄). Concentration in vacuo followed by chromatography (CHCl₃–MeOH, 200:1) yielded a mixture of **17** and **18** (total 68.5 mg, 69%) in a ratio of 6.4:1 (based on ¹H NMR) as a colorless oil. This mixture was separated by further chromatography (Et₂O–MeOH, 200:1) and the first fractions gave (2*R*,4*aR*,5*S*)-5-(benzyloxy)-2-[3-(methoxymethoxy)propyl]-4*a*,5,6,7-tetrahydropyrido[1,2-*b*][1,2]oxazin-8(2*H*)-one (**17**) as a colorless oil: [α]_D²² –46.3 (c 1.18, CHCl₃); IR (neat) 1674 cm^{–1}; ¹H NMR (400 MHz, CDCl₃) δ 1.59–1.83 (m, 4H), 1.88–2.05 (m, 1H), 2.13–2.24 (m, 1H), 2.36 (ddd, J = 18.2, 5.9, 12.4 Hz, 1H), 2.58 (ddd, J = 17.4, 5.5, 3.1 Hz, 1H), 3.32 (s, 3H), 3.41 (ddd, J = 10.9, 3.4, 8.8 Hz, 1H), 3.46–3.53 (m, 1H), 3.53–3.62 (m, 1H), 4.21 (dd, J = 8.8, 1.3 Hz, 1H), 4.37 (br s, 1H),

4.54 and 4.68 (ABq, $J = 11.5$ Hz, 2H), 4.58 (s, 2H), 5.91 (ddd, $J = 10.3, 3.5, 2.1$ Hz, 1H), 5.98 (d, $J = 10.3$ Hz, 1H), 7.29–7.39 (m, 5H); ^{13}C NMR (100.6 MHz, CDCl_3) δ 25.2, 26.2, 28.9, 30.6, 55.1, 60.4, 67.4, 71.5, 76.4, 78.9, 96.3, 123.6, 127.7 (2 carbons), 128.0, 128.5 (2 carbons), 128.7, 137.4, 164.8; HRMS (ESI-TOF) m/z Calcd for $\text{C}_{20}\text{H}_{27}\text{NO}_5\text{Na}$ $[\text{M} + \text{Na}]^+$ 384.1787, found 384.1804.

The second fractions gave (2*S*,4*aS*,5*S*)-5-(benzyloxy)-2-[3-(methoxymethoxy)propyl]-4*a*,5,6,7-tetrahydropyrido[1,2-*b*][1,2]oxazin-8(2*H*)-one (**18**) as a colorless oil: IR (neat) 1670 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 1.60–1.85 (m, 4H), 1.85–2.05 (m, 1H), 2.05–2.15 (m, 1H), 2.37 (d, $J = 16.1$ Hz, 1H), 2.53–2.75 (m, 1H), 3.29 (s, 3H), 3.40–3.60 (m, 3H), 4.35 (br s, 1H), 4.37–4.46 (m, 1H), 4.43 and 4.61 (ABq, $J = 11.8$ Hz, 2H), 4.54 (s, 2H), 5.62 (dd, $J = 10.3, 1.0$ Hz, 1H), 5.70–5.90 (m, 1H), 7.20–7.35 (m, 5H); ^{13}C NMR (100.6 MHz, CDCl_3) δ 23.2, 26.1, 27.9, 30.3, 55.0, 60.7, 67.4, 70.6, 72.9, 78.8, 96.2, 123.0, 127.2 (2 carbons), 127.6, 128.3 (2 carbons), 128.8, 137.7, 165.1; HRMS (ESI-TOF) m/z Calcd for $\text{C}_{20}\text{H}_{27}\text{NO}_5\text{Na}$ $[\text{M} + \text{Na}]^+$ 384.1787, found 384.1794.

(2*S*,4*aR*,5*S*,7*S*)-5-(Benzyloxy)-7-hydroxy-2-[3-(methoxymethoxy)propyl]hexahydropyrido[1,2-*b*][1,2]oxazin-8(2*H*)-one (19): ^1H NMR (300 MHz, CDCl_3) δ 1.55–2.00 (m, 7H), 2.05–2.25 (m, 1H), 2.43–2.55 (m, 1H), 3.35 (s, 3H), 3.40–3.65 (m, 4H), 3.85–3.95 (m, 1H), 4.15–4.25 (m, 1H), 4.37–4.47 (m, 1H), 4.50–4.65 (m, 2H), 4.60 (s, 2H), 7.27–7.43 (m, 5H).

(2*S*,4*aR*,5*S*,7*S*)-5-(Benzyloxy)-7-[[*tert*-butyl(diphenyl)silyl]oxy]-2-[3-(methoxymethoxy)propyl]hexahydropyrido[1,2-*b*][1,2]oxazin-8(2*H*)-one (20): IR (neat) 1685 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 1.09 (s, 9H), 1.58–1.78 (m, 5H), 1.88–2.13 (m, 5H), 3.34 (s, 3H), 3.46–3.53 (m, 1H), 3.56–3.66 (m, 2H), 4.20 (dd, $J = 13.5, 5.2$ Hz, 1H), 4.28 and 4.39 (ABq, $J = 11.6$ Hz, 2H), 4.38 (dd, $J = 5.7, 2.2$ Hz, 1H), 4.60 (s, 2H), 7.17–7.20 (m, 2H), 7.27–7.48 (m, 9H), 7.68–7.81 (m, 4H); ^{13}C NMR (100.6 MHz, CDCl_3) δ 19.4, 24.3, 26.7, 26.9 (3 carbons), 27.0, 32.9, 55.2, 62.9, 67.6, 69.1, 71.1, 74.5, 77.3, 79.0, 96.4, 127.6 (2 carbons), 127.7 (2 carbons), 127.8 (2 carbons), 127.9, 128.5 (2 carbons), 129.9, 130.0, 132.3, 134.1, 135.8 (2 carbons), 136.2 (2 carbons), 137.6, 164.7; HRMS (ESI-TOF) m/z Calcd for $\text{C}_{36}\text{H}_{47}\text{NO}_6\text{SiNa}$ $[\text{M} + \text{Na}]^+$ 640.3070, found 640.3113.

(2*S*,4*aR*,5*S*,7*S*,8*S*)-5-(Benzyloxy)-7-[[*tert*-butyl(diphenyl)silyl]oxy]-2-[3-(methoxy-

methoxy)propyl]-8-methyloctahydropyrido[1,2-*b*][1,2]oxazine (23): ^1H NMR (500 MHz, CDCl_3) δ 1.10 (s, 12H), 1.28–1.36 (m, 1H), 1.48–1.71 (m, 4H), 1.87–1.92 (m, 2H), 2.06–2.12 (m, 1H), 2.16 (dt, $J = 12.9, 3.6$ Hz, 1H), 2.35–2.48 (m, 2H), 2.70–2.80 (m, 1H), 3.37 (s, 3H), 3.50–3.67 (m, 3H), 3.91 (dt, $J = 9.3, 4.8$ Hz, 1H), 4.06 (m, 1H), 4.19 and 4.26 (ABq, $J = 11.4$ Hz, 2H), 4.62 (s, 2H), 7.20–7.34 (m, 5H), 7.36–7.47 (m, 6H), 7.71–7.76 (m, 4H); ^{13}C NMR (125 MHz, CDCl_3) δ 14.2, 16.7, 19.8, 23.2, 26.5, 27.2 (3 carbons), 28.1, 36.7, 55.1, 63.6, 67.9, 69.2, 71.4, 71.7, 75.9, 76.0, 96.4, 127.5 (2 carbons), 127.6 (4 carbons), 127.8, 128.3 (2 carbons), 129.6, 129.7, 134.0, 134.5, 136.0 (2 carbons), 136.1 (2 carbons), 138.6; HRMS (ESI-TOF) m/z Calcd for $\text{C}_{37}\text{H}_{51}\text{NO}_5\text{Si}$ [$\text{M} + \text{H}$] $^+$ 618.3615, found 618.3593.

(3*S*)-1-((2*R*,3*S*,5*S*,6*S*)-3-(Benzyloxy)-5-[[*tert*-butyl(diphenyl)silyl]oxy]-6-methylpiperidin-2-yl)-6-(methoxymethoxy)hexan-3-ol (24): IR (neat) 3388 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 1.04 (3H, d, $J = 6.7$ Hz), 1.11 (9H, s), 1.24 (t, $J = 13.1$ Hz, 1H), 1.28–1.41 (m, 1H), 1.43–1.58 (m, 2H), 1.59–1.82 (m, 4H), 2.07–2.22 (m, 2H), 2.57 (td, $J = 9.5, 2.4$ Hz, 1H), 2.67 (q, $J = 6.6$ Hz, 1H), 3.33–3.40 (m, 1H), 3.36 (s, 3H), 3.52–61 (m, 2H), 3.61–3.68 (m, 1H), 3.98 (br s, 1H), 4.11 and 4.19 (ABq, $J = 11.4$ Hz, 2H), 4.63 (s, 2H), 7.18–7.23 (m, 2H), 7.23–7.34 (m, 3H), 7.35–7.49 (m, 6H), 7.63–7.75 (m, 4H); ^{13}C NMR (100.6 MHz, CDCl_3) δ 18.5, 19.6, 26.4, 27.3 (3 carbons), 28.5, 33.9, 34.2, 37.1, 55.2, 55.3, 60.3, 68.1, 70.2, 70.7, 72.1, 76.2, 96.4, 127.5, 127.6 (2 carbons), 127.7 (4 carbons), 128.4 (2 carbons), 129.8, 129.9, 133.4, 134.5, 136.1 (4 carbons), 138.6; HRMS (ESI-TOF) m/z Calcd for $\text{C}_{37}\text{H}_{53}\text{NO}_5\text{Si}$ [$\text{M} + \text{H}$] $^+$ 620.3771, found 620.3752.

Benzyl (2*S*,3*S*,5*S*,6*R*)-3-[[*tert*-Butyl(diphenyl)silyl]oxy]-5-hydroxy-6-[(3*S*)-3-hydroxy-6-(methoxymethoxy)hexyl]-2-methylpiperidine-1-carboxylate (25): IR (neat) 3440, 1671 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 1.07 (s, 9H), 1.12–1.80 (m, 14H), 1.80–1.96 (m, 1H), 3.35 (s), 3.48–3.58 (m, 2H), 3.60–3.78 (m, 1H), 3.82 (br s, 1H), 4.05 (br s, 1H), 4.20–4.42 (m, 2H), 4.61 (s, 2H), 4.98 and 5.12 (ABq, $J = 12.0$ Hz, 2H), 7.24–7.46 (m, 10H), 7.58–7.72 (m, 5H); HRMS (ESI-TOF) m/z Calcd for $\text{C}_{38}\text{H}_{53}\text{NO}_7\text{SiNa}$ [$\text{M} + \text{Na}$] $^+$ 686.3489, found 686.3435.

Benzyl (2*S*,3*S*,5*S*,6*R*)-3-[[*tert*-Butyl(diphenyl)silyl]oxy]-6-[(3*S*)-6-(methoxymethoxy)-3-[[[(methylsulfanyl)carbothioyl]oxy]hexyl]-2-methyl-5-[[[(methylsulfanyl)carbothioyl]oxy]piperidine-1-carboxylate (26): IR (neat) 1696 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 1.06 (9H, s), 1.25–1.35 (m, 4H), 1.45–1.93 (m, 9H), 2.15–2.23 (m, 3H), 2.55 (s, 3H), 3.35 (s,

3H), 3.44–3.56 (m, 2H), 4.10 (quint, $J = 5.5$ Hz, 1H), 4.23–4.35 (m, 1H), 4.40–4.55 and 4.66–4.76 (each m, total 1H), 4.60 (s, 2H), 5.09 (s, 2H), 5.49 and 5.60 (each s, total 1H), 5.62–5.76 (m, 1H), 7.25–7.45 (m, 10H), 7.55–7.65 (m, 5H); ^{13}C NMR (100.6 MHz, CDCl_3) δ 13.9, 14.1, 18.4, 19.0, 19.2, 25.5, 26.9 (3 carbons), 27.8, 29.2, 29.4, 30.5, 30.8, 50.6, 50.8, 53.8, 55.3, 66.0, 66.1, 67.2, 77.3, 96.5, 127.6, 127.7 (4 carbons), 127.8 (2 carbons), 128.0, 128.5 (4 carbons), 129.9 (2 carbons), 135.7 (4 carbons), 213.9, 216.1; HRMS (ESI–TOF) m/z Calcd for $\text{C}_{42}\text{H}_{57}\text{NO}_7\text{S}_4\text{SiNa}$ $[\text{M} + \text{Na}]^+$ 866.2685, found 866.2657.

Benzyl (2S,3S,6R)-3-[[*tert*-Butyl(diphenyl)silyl]oxy]-6-[6-(methoxymethoxy)hexyl]-2-methylpiperidine-1-carboxylate (27): IR (neat) 1695 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 0.93 (t, $J = 7.3$ Hz, 3H), 1.06 (s, 9H), 1.13–1.43 (m, 8H), 1.43–1.60 (m, 3H), 1.60–1.84 (m, 3H), 3.35 (s, 3H), 3.49 (t, $J = 6.4$ Hz, 2H), 3.68–3.80 (m, 1H), 3.97–4.08 (m, 1H), 4.29 and 4.50 (each br s, total 1H in 1:1 ratio), 4.61 (s, 2H), 5.05 (br s, 2H), 7.20–7.47 (m, 10H), 7.60–7.70 (m, 5H); HRMS (ESI–TOF) m/z Calcd for $\text{C}_{38}\text{H}_{53}\text{NO}_5\text{SiNa}$ $[\text{M} + \text{Na}]^+$ 654.3591, found 654.3558.

Benzyl (2S,3S,6R)-3-[[*tert*-Butyl(diphenyl)silyl]oxy]-6-(6-hydroxyhexyl)-2-methylpiperidine-1-carboxylate (28): $[\alpha]_D^{21} -37.4$ (c 1.12, CHCl_3); IR (neat) 3443, 1693 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 1.07 (s, 9H), 1.10–1.85 (m, 17H), 3.60 (br s, 2H), 3.74 (br t, $J = 6.0$ Hz, 1H), 3.85–4.08 (m, 1H), 4.30 and 4.50 (each br s, total 1H in 1:1 ratio), 5.06 (br s, 2H), 7.23–7.50 (m, 10H), 7.57–7.72 (m, 5H); ^{13}C NMR (100.6 MHz, CDCl_3) δ 13.6, 17.6, 19.2, 23.2, 25.6, 26.0, 27.0 (3 carbons), 27.3, 29.0, 32.7, 49.8, 51.1, 62.9, 66.8, 71.3, 77.3, 127.6 (2 carbons), 127.7 (2 carbons), 127.8, 128.4 (4 carbons), 129.7, 129.8, 135.6 (2 carbons), 135.7 (4 carbons), 155.7; HRMS (ESI–TOF) m/z Calcd for $\text{C}_{36}\text{H}_{49}\text{NO}_4\text{Si}$ $[\text{M} + \text{H}]^+$ 588.3509, found 588.3473.

6-[(2R,5S,6S)-1-[(Benzyloxy)carbonyl]-5-hydroxy-6-methylpiperidin-2-yl]hexanoic Acid (29): $[\alpha]_D^{22} -8.81$ (c 1.22, CHCl_3); IR (neat) 3414, 1667 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 1.17 (d, $J = 7.0$ Hz, 3H), 1.20–1.35 (m, 4H), 1.48–1.76 (m, 8H), 2.29 (t, $J = 7.4$ Hz, 2H), 3.74–3.80 (m, 1H), 4.06–4.15 (m, 1H), 4.50 (quint, $J = 6.6$ Hz, 1H), 5.10 and 5.15 (ABq, $J = 12.4$ Hz, 2H), 7.27–7.38 (m, 5H); ^{13}C NMR (100.6 MHz, CDCl_3) δ 13.7, 22.9, 24.6, 26.5, 27.0, 29.0, 33.9, 34.7, 49.9, 50.8, 67.3, 69.8, 127.95 (2 carbons), 128.03, 128.5 (2 carbons), 136.8, 156.0, 178.9; HRMS (ESI–TOF) m/z Calcd for $\text{C}_{20}\text{H}_{29}\text{NO}_5\text{Na}$ $[\text{M} + \text{Na}]^+$ 386.1943, found

386.1955.

6-[(2*R*,5*S*,6*S*)-5-Hydroxy-6-methylpiperidin-2-yl]hexanoic Acid [Azimic Acid (3**):** mp 212–215 °C; $[\alpha]^{23}_D +7.45$ (*c* 0.49, MeOH); ^1H NMR (500 MHz, CD_3OD) δ 1.37 (d, *J* = 6.7 Hz, 3H), 1.40–1.89 (m, 11H), 1.95–2.03 (m, 1H), 2.35 (t, *J* = 7.3 Hz, 2H), 3.08–3.15 (m, 1H), 3.29 (q, *J* = 6.7 Hz, 1H), 3.88 (t, *J* = 1.5 Hz, 1H); ^{13}C NMR (125 MHz, CDCl_3) δ 15.9, 23.5, 25.7, 25.9, 29.8, 31.0, 34.5, 34.7, 57.6, 58.6, 65.8, 177.5; HRMS (ESI–TOF) *m/z* Calcd for $\text{C}_{12}\text{H}_{24}\text{NO}_3$ $[\text{M} + \text{H}]^+$ 230.1756, found 230.174.

Dibenzyl (1*S*,9*R*,11*S*,12*S*,20*R*,22*S*)-11,22-Dimethyl-3,14-dioxo-2,13-dioxo-10,21-diazatricyclo[18.2.2.2^{9,12}]hexacosane-10,21-dicarboxylate (30**):** To a solution of **29** (100 mg, 0.275 mmol) in THF (5 mL) were added Et_3N (42 mg, 0.42 mmol) and 2,4,6-trichlorobenzoyl chloride (101 mg, 0.414 mmol) and the mixture was stirred at room temperature for 3 h. The resulting insoluble material was removed by filtration and the filtrate was concentrated in vacuo. The residual oil was dissolved in toluene (138 mL). To the solution was added 4-(dimethylamino)pyridine (168 mg, 1.38 mmol) and the mixture was heated at reflux for 36 h. After being cooled to room temperature, the mixture was diluted with Et_2O (100 mL), washed with 1 M aqueous HCl (50 mL), saturated aqueous NaHCO_3 (50 mL), and water (50 mL), and dried (MgSO_4). Concentration in vacuo and purification of the residue by column chromatography on silica gel (hexane–EtOAc, 20:1) gave **30** (67.6 mg, 71%) as a colorless oil: $[\alpha]^{24}_D -19.0$ (*c* 0.43, CHCl_3); IR (neat) 1736, 1694 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3 , amide rotamers) δ 1.16 (d, *J* = 7.0 Hz, 1.5H), 1.21 (d, *J* = 7.0 Hz, 4.5H), 1.23–1.86 (m, 24H), 2.20–2.42 (m, 4H), 4.15 (br s, 0.5H), 4.20 (br s, 1.5H), 4.58 (quint, *J* = 6.7 Hz, 0.5H), 4.65 (quint, *J* = 7.0 Hz, 1.5H), 4.78–4.92 (m, 2H), 5.14 (br s, 4H), 7.28–7.39 (m, 10H); ^{13}C NMR (100.6 MHz, CDCl_3 , amide rotamers) δ 16.2 (2 carbons), 20.1 (2 carbons), 24.5 (2 carbons), 24.8 (2 carbons), 25.6 and 25.8 (2 carbons in 3:1 ratio), 28.7 (2 carbons), 33.6 (2 carbons), 34.7 (2 carbons), 47.9 and 48.2 (2 carbons in 3:1 ratio), 49.8 and 50.1 (2 carbons in 4.3:1 ratio), 67.2 (2 carbons), 70.7 (2 carbons), 71.2 (2 carbons), 127.9 (2 carbons), 128.0 (2 carbons), 128.5 (2 carbons), 136.7 (2 carbons), 155.7 (2 carbons), 172.1 and 172.5 (2 carbons in 3:1 ratio); EIMS *m/z* (relative intensity) 691 (MH^+ , 20), 647 (68), 557 (24), 312 (85), 284 (100), 202 (100); HRMS (ESI–TOF) *m/z* Calcd for $\text{C}_{40}\text{H}_{54}\text{N}_2\text{O}_8\text{Na}$ $[\text{M} + \text{Na}]^+$ 713.3778, found 713.3793.

(1S,9R,11S,12S,20R,22S)-11,22-Dimethyl-2,13-dioxo-10,21-diazatricyclo[18.2.2.2^{9,12}]-hexacosane-3,14-dione [Azimine (1)]: mp 110–111 °C; $[\alpha]_D^{23} +3.14$ (c 0.74, EtOH); IR (neat) 3389, 1734 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 1.04 (d, $J = 6.6$ Hz, 6H), 1.10–1.80 (m, 22H), 2.04 (dq, $J = 14.3, 2.9$ Hz, 2H), 2.28–2.50 (m, 4H), 2.58–2.70 (m, 2H), 2.86 (q, $J = 6.1$ Hz, 2H), 4.76 (s, 2H); EIMS m/z (relative intensity) 423 (MH^+ , 92), 379 (31), 307 (14), 212 (100), 97 (40); HRMS (ESI–TOF) m/z Calcd for $\text{C}_{24}\text{H}_{43}\text{N}_2\text{O}_4$ $[\text{M} + \text{H}]^+$ 423.3223, found 423.3203.

Benzyl (2S,3S,6R)-3-[[*tert*-Butyl(diphenyl)silyl]oxy]-6-[(6*E*)-8-ethoxy-8-oxooct-6-enyl]-2-methylpiperidine-1-carboxylate (31): $[\alpha]_D^{21} -32.9$ (c 1.60, CHCl_3); IR (neat) 1719, 1695 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3 , amide rotamers) δ 1.06 (s, 9H), 1.10–1.80 (m, 15H), 1.29 (t, $J = 7.1$ Hz, 3H), 2.04–2.20 (br m, 2H), 3.73 (br t, $J = 5.7$ Hz, 1H), 3.86–4.03 (m, 1H), 4.18 (q, $J = 7.1$ Hz, 2H), 4.29 (br s, 0.5H), 4.49 (br s, 0.5H), 5.05 (br s, 2H), 5.78 (d, $J = 15.7$ Hz, 1H), 6.86–7.00 (m, 1H), 7.27–7.45 (m, 10H), 7.58–7.70 (m, 5H); HRMS (ESI–TOF) m/z Calcd for $\text{C}_{40}\text{H}_{53}\text{NO}_5\text{SiNa}$ $[\text{M} + \text{Na}]^+$ 678.3591, found 678.3550.

Benzyl (2S,3S,6R)-3-[[*tert*-Butyl(diphenyl)silyl]oxy]-6-(8-ethoxy-8-oxooctyl)-2-methylpiperidine-1-carboxylate (32): $[\alpha]_D^{22} -27.9$ (c 1.24, CHCl_3); IR (neat) 1734, 1696 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3 , amide rotamers) δ 1.06 (s, 9H), 1.10–1.65 (m, 18H), 1.25 (t, $J = 7.2$ Hz, 3H), 1.72 (br s, 1H), 2.27 (t, $J = 7.6$ Hz, 2H), 3.68–3.78 (m, 1H), 3.85–4.07 (m, 1H), 4.15–4.60 (m, 1H), 5.05 (br s, 2H), 7.20–7.48 (m, 10H), 7.58–7.72 (m, 5H); HRMS (ESI–TOF) m/z Calcd for $\text{C}_{40}\text{H}_{55}\text{NO}_5\text{SiNa}$ $[\text{M} + \text{Na}]^+$ 680.3747, found 680.3701.

8-[(2*R*,5*S*,6*S*)-1-[(Benzyloxy)carbonyl]-5-hydroxy-6-methylpiperidinyl]octanoic Acid (6): $[\alpha]_D^{22} -11.0$ (c 2.09, CHCl_3); IR (neat) 1696, 1666 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 1.17 (d, $J = 7.0$ Hz, 3H), 1.20–1.36 (br m, 8H), 1.47–1.55 (m, 2H), 1.57–1.75 (m, 6H), 2.33 (t, $J = 7.5$ Hz, 2H), 3.73–3.80 (m, 1H), 4.11 (br m, 1H), 4.50 (quint, $J = 6.7$ Hz, 1H), 5.11 and 5.16 (ABq, $J = 12.4$ Hz, 2H), 7.28–7.38 (m, 5H); HRMS (ESI–TOF) m/z Calcd for $\text{C}_{22}\text{H}_{33}\text{NO}_5\text{Na}$ $[\text{M} + \text{Na}]^+$ 414.2256, found 414.2236.

Dibenzyl (1S,11*R*,13*S*,14*S*,24*R*,26*S*)-13,26-Dimethyl-3,16-dioxo-2,15-dioxo-12,25-diazatricyclo[22.2.2.2^{11,14}]triacontane-12,25-dicarboxylate (5): The same experimental procedure described for the preparation of **30** was applied to **6** (75.6 mg, 0.193 mmol).

Purification of the crude product by chromatography (hexane–AcOEt, 20:1) afforded 50.9 mg (71%) of **5** as a colorless oil: $[\alpha]_D^{22} -17.7$ (*c* 2.55, CHCl₃); IR (neat) 1734, 1696 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 1.18 (d, *J* = 7.0 Hz, 6H), 1.20–1.33 (m, 14H), 1.43–1.83 (m, 18H), 2.23–2.35 (m, 4H), 4.17 (br m, 2H), 4.58 (br m, 2H), 4.85 (br m, 2H), 5.13 (br s, 4H), 7.28–7.37 (m, 10H); HRMS (ESI–TOF) *m/z* Calcd for C₄₄H₆₂N₂O₈Na [M + Na]⁺ 769.4404, found 769.4383.

(1S,11R,13S,14S,24R,26S)-13,26-Dimethyl-2,15-dioxo-12,25-diazatricyclo[22.2.2.2^{11,14}]-triacontane-3,16-dione [Carpaine (2**)]:** mp 119–120 °C; $[\alpha]_D^{22} +20.9$ (*c* 0.34, EtOH); ¹H NMR (500 MHz, CDCl₃) δ 1.05 (d, *J* = 6.6 Hz, 6H), 1.08–1.67 (m, 30H), 1.95–2.10 (m, 2H), 2.27–2.38 (m, 2H), 2.39–2.48 (m, 2H), 2.59 (br m, 2H), 2.87 (q, *J* = 6.3 Hz, 2H), 4.77 (br s, 2H); ¹³C NMR (125 MHz, CDCl₃) 18.8, 25.4, 25.6, 26.5, 28.77, 28.81, 29.2, 29.8, 34.7, 37.5, 53.7, 56.1, 70.4, 173.5; HRMS (ESI–TOF) *m/z* Calcd for C₂₈H₅₀N₂O₄ [M + H]⁺ 479.3849, found 479.3862.