The Effect of Varying Substituents on the Equilibrium Distribution and Conformation of Macrocyclic Steroidal N–Acyl Hydrazones

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Supporting Information 1. Characterisation data

Monomer 3

Found: C, 67.73; H, 8.74; N, 4.68. $C_{34}H_{52}N_2O_6 \cdot H_2O$ requires C, 67.77; H, 8.97; N, 4.65, R_f = 0.4 (10%MeOH/$CHCl_3$), ν_{max}/cm^{-1} ($CDCl_3$) 3617, 3450, 1700, 1672; δ_H (400 MHz, $CDCl_3$) 0.69 (s, 3H, 18–Me), 0.96 (s, 3H, 19–Me), 0.99 (d, *J* = 6.1 Hz, 3H, 21–Me), 3.34 (s, 6H, $CH(OMe)_2$), 3.90 (brs, 2H, $CONHNH_2$), 4.00 (brs, 1H, 12βH), 4.97 (tt, *J* = 4.5, 11.3 Hz, 1H, 3βH), 5.43 (s, 1H, $CH(OMe)_2$), 6.84 (brs, 1H, $CONHNH_2$), 7.43 (t, *J* = 7.7 Hz, 1H, H_ε), 7.64 (d, *J* = 7.7 Hz, 1H, H_δ), 8.00 (d, *J* = 7.7 Hz, 1H, H_η), 8.09 (s, 1H, H_γ); δ_C (100 MHz, $CDCl_3$) 12.8, 17.4, 23.2, 23.6, 26.0, 26.7, 27.0, 27.5, 28.9, 31.3, 31.5, 32.3, 33.8, 34.2, 35.0, 35.2, 36.0, 42.0, 46.5, 47.2, 48.4, 52.8, 52.8, 73.2, 75.0, 102.7, 128.0, 128.3, 129.8, 131.0, 131.0, 138.5, 166.0, 174.4; ESI–MS: m/z 607 $[M+Na]^+$, found 607.3742, $C_{34}H_{52}N_2O_6Na$ requires 607.3723.

Monomer 4

Found: C, 68.77; H, 7.98; N, 5.92, $C_{40}H_{55}N_3O_7 \cdot 0.5H_2O$ requires C, 68.76; H, 8.02; N, 6.01, R_f = 0.34 (10%MeOH/$CHCl_3$), ν_{max}/cm^{-1} ($CDCl_3$) 3448, 1715, 1673; δ_H (400 MHz, $CDCl_3$) 0.79 (d, *J* = 6.0 Hz, 3H, 21–Me), 0.80 (s, 3H, 18–Me), 0.94 (s, 3H, 19–Me), 3.31 (s, 6H, $CH(OMe)_2$), 3.83 (br, 2H, $CONHNH_2$), 4.87 (m, 1H, 3βH), 5.38 (m, 1H, 12βH), 5.40 (s, 1H, $CH(OMe)_2$), 6.72 (br, 1H, $CONHNH_2$) 7.41 (t, *J* = 7.7 Hz, 1H, H_ε), 7.62 (d, *J* = 7.7 Hz, 1H, H_δ), 7.80 (d, *J* = 7.7 Hz, 1H, H_η), 7.88 (d, *J* = 6.0 Hz, 2H, β–pyridyl), 7.98 (s, 1H, H_γ), 8.82 (d, *J* = 6.0 Hz, 2H, α–pyridyl); δ_C (100 MHz, $CDCl_3$) 12.6, 17.6, 23.1, 23.5, 25.6, 25.9, 26.0, 26.6, 26.8, 27.4, 31.3, 31.4, 32.3, 34.1, 34.7, 34.9, 35.7, 41.8, 45.6, 46.5, 48.2, 50.1, 52.8, 52.8, 74.6, 77.7, 102.6, 122.7, 127.8, 128.3, 129.5, 130.8, 131.1, 137.9, 138.6, 150.8, 164.4, 165.9, 174.0; ESI–MS: m/z 712 $[M+Na]^+$, found 712.3955, $C_{40}H_{55}N_3O_7Na$ requires 712.3938.

Monomer 5

Found: C, 68.21; H, 7.67; N, 5.35 $C_{43}H_{57}N_3O_8{\cdot}0.5H_2O$ requires C, 68.60; H, 7.71; N, 5.58, R_f = 0.32 (200:10:1 DCM/EtOH/NH_3), ν_{max}/cm^{-1} ($CDCl_3$) 3426, 1710, 1702; δ_H (400 MHz, $CDCl_3$) 0.81 (d, *J* = 6.0 Hz, 3H, 21–Me), 0.82 (s, 3H, 18–Me), 0.98 (s, 3H, 19–Me), 1.45 (s, 9H, CO_2CMe_3), 4.92 (tt, *J* = 5.3, 10.9 Hz, 1H, 3βH), 5.40 (m, 1H, 12βH), 6.46 (brs, 1H, CONHNH), 7.16 (brs, 1H, CONHNH), 7.60 (t, *J* = 7.7 Hz, 1H, H_ε), 7.89 (dd, *J* = 1.6, 4.4 Hz, 2H, β–pyridyl), 8.06 (dt, *J* = 1.4, 7.7 Hz, 1H, H_δ), 8.09 (dt, *J* = 1.4, 7.7 Hz, 1H, H_η), 8.38 (t, *J* = 1.4 Hz, 1H, H_γ), 8.84 (dd, *J* = 1.6, 4.4 Hz, 2H, α–pyridyl), 10.07 (s, 1H, CHO); δ_C (100 MHz, $CDCl_3$) 12.6, 17.6, 23.0, 23.5, 25.8, 26.0, 26.5, 26.8, 27.4, 28.1, 31.0, 32.2, 34.0, 34.7 (2), 34.8, 35.7, 41.7, 45.5, 48.2, 50.2, 75.1, 77.7, 81.8, 122.7, 129.2, 130.8, 131.8, 133.3, 134.9, 136.5, 137.9, 150.8, 155.4, 164.4, 164.8, 172.6, 191.5; ESI–MS: m/z 766 $[M+Na]^+$, found 766.3998, $C_{43}H_{57}N_3O_8Na$ requires 766.4043.

Monomer 6

Found: C, 68.79; H, 8.08; N, 5.88. $C_{40}H_{55}N_3O_7{\cdot}0.5H_2O$ requires C, 68.76; H, 8.02; N, 6.01, R_f = 0.36 (10%MeOH/$CHCl_3$), ν_{max}/cm^{-1} ($CDCl_3$) 3449, 1712, 1672; δ_H (400 MHz, $CDCl_3$) 0.78 (d, *J* = 6.0 Hz, 3H, 21–Me), 0.80 (s, 3H, 18–Me), 0.94 (s, 3H, 19–Me), 3.36 (s, 6H, CH(**OMe**)$_2$), 3.81 (br, 2H, CONH**NH$_2$**), 4.87 (m, 1H, 3βH), 5.40 (m, 1H, 12βH), 5.42 (s, 1H, C**H**(OMe)$_2$), 6.65 (br, 1H, CO**NH**NH_2) 7.49 (d, *J* = 8.0 Hz, 2H, H_ε), 7.85 (d, *J* = 8.0 Hz, 2H, H_δ), 7.88 (d, *J* = 6.0 Hz, 2H, β–pyridyl), 8.84 (d, *J* = 6.0 Hz, 2H, α–pyridyl); δ_C (100 MHz, $CDCl_3$) 12.6, 17.6, 23.0, 23.5, 25.8, 26.0, 26.5, 26.8, 27.4, 31.3, 31.4, 32.3, 34.0, 34.7, 34.9, 35.7, 41.7, 45.5, 48.2, 50.2, 52.6, 74.5, 77.7, 102.3, 122.7, 126.7, 129.3, 130.7, 137.9, 142.8, 150.8, 164.3, 165.7, 174.0; ESI–MS: m/z 690 $[M+H]^+$, 712 $[M+Na]^+$, found 712.3921, $C_{40}H_{55}N_3O_7Na$ requires 712.3938.

Monomer 7

Found: C, 68.86; H, 8.86; N, 4.70. $C_{34}H_{53}N_2O_6{\cdot}0.5\ H_2O$ requires C, 68.80; H, 8.93; N, 4.72, R_f = 0.4 (10%MeOH/$CHCl_3$), ν_{max}/cm^{-1} ($CDCl_3$) 3617, 3450, 1707, 1672; δ_H (400 MHz, $CDCl_3$) 0.68 (s, 3H, 18–Me), 0.93 (s, 3H, 19–Me), 0.97 (d, *J* = 6.2 Hz, 3H, 21–Me), 3.31 (s, 6H, CH(OMe)$_2$), 3.89 (brs, 2H, CONHNH_2), 4.00 (brs, 1H, 12βH), 4.95 (tt, *J* = 4.5, 11.3 Hz, 1H, 3βH), 5.43 (s, 1H, CH(OMe)$_2$), 6.82 (brs, 1H, CONHNH_2), 7.50 (d, *J* = 8.3 Hz, 2H, H_ε), 8.02 (d, *J* = 8.3 Hz, 2H, H_δ); δ_C (100 MHz, $CDCl_3$) 12.8, 17.4, 23.2, 23.6, 26.0, 26.7, 27.0, 27.5, 28.9, 31.3, 31.5, 32.3, 33.8, 34.2, 34.9, 35.2, 36.0, 41.9, 46.5, 47.2, 48.4, 52.6, 73.2, 74.9, 102.4, 126.7, 129.5, 130.9, 142.7, 165.9, 174.4; ESI–MS: m/z 607 $[M+Na]^+$, found 607.3719, $C_{34}H_{52}N_2O_6Na$ requires 607.3723.

Macrocycle 8

δ_H (400 MHz, $CDCl_3$) 0.68 (s, 3H, 18–Me), 0.91 (s, 3H, 19–Me), 1.19 (d, *J* = 6.0 Hz, 3H, H–21), 2.57 (m, 1H, 23–H), 2.96 (m, 1H, 23–H), 3.90 (m, 1H, 12βH), 4.87 (tt, *J* = 5.2, 10.1 Hz, 1H, 3βH), 7.30 (d, *J* = 7.7 Hz, 1H, H_δ), 7.42 (t, *J* = 7.7 Hz, 1H, H_ε), 7.55 (s, 1H, H_μ), 8.08 (d, *J* = 7.7 Hz, 1H, H_η), 8.51 (s, 1H, H_γ), 9.34 (brs, 1H, NH_{cis}); δ_C (100 MHz, $CDCl_3$) 12.9, 18.4, 23.3, 23.9, 26.1, 27.0, 27.7, 29.0, 29.6, 31.6, 32.3, 33.7, 34.3, 35.1, 35.5, 36.1, 42.0, 44.9, 45.9, 46.5, 48.2, 73.0, 76.0, 124.7, 128.7, 131.3, 131.4, 133.6, 133.9, 141.8, 165.6, 177.4; ESI–MS: m/z 1063 $[M+Na]^+$, found 1063.6417, $C_{64}H_{88}N_4O_8$ requires 1063.6494.

Macrocycle 9

ν_{max}/cm^{-1} ($CDCl_3$) 1717; δ_H (400 MHz, $CDCl_3$) 0.87 (s, 3H, 18–Me), 0.95–0.97 (m, 6H, 21–Me, 19–Me), 4.91 (tt, *J* = 5.3, 10.8 Hz, 1H, 3βH), 5.52 (m, 1H, 12βH), 7.43 (t, *J* = 7.7 Hz, 1H, H_ε), 7.85 (s, 1H, H_γ), 7.87 (d, *J* = 7.7 Hz, 1H, H_η), 7.90 (d, *J* = 5.9 Hz, 2H, β–pyridyl), 8.01 (d, *J* = 7.7 Hz, 2H, H_δ), 8.62 (s, 1H, H_θ), 8.65 (d, *J* = 5.9 Hz, 2H, α–pyridyl), 10.85 (s, 1H, NH_{trans}); δ_C (100 MHz, $CDCl_3$) 12.7, 18.0, 22.9, 23.3, 25.8, 25.9, 26.3, 26.4, 27.2, 30.6, 30.9, 32.1, 33.7, 34.3, 34.6, 35.6, 41.4, 45.3, 47.2, 50.6, 74.3, 78.1, 123.1, 127.6, 128.9, 130.9, 131.1, 131.7, 132.3, 134.7, 138.7, 148.2, 150.3, 163.6, 164.9, 171.2; ESI–MS: m/z 1251 $[M+H]^+$, 1273 $[M+Na]^+$, found 1251.7046, $C_{76}H_{95}N_6O_{10}$ requires 1251.7104.

Macrocycle 10

ν_{max}/cm^{-1} ($CDCl_3$) 1716, 1674; δ_H (400 MHz, $CDCl_3$) 0.84 (m, 6H, 18, 21–Me), 1.02 (s, 3H, 19–Me), 2.33 (m, 1H, 23–H), 2.75 (m, 1H, 23–H), 4.75 (m, 1H, 3βH), 5.33 (m, 1H, 12βH), 7.19 (d, *J* = 8.2 Hz, 2H, H_ε), 7.61 (d, *J* = 8.2 Hz, 2H, H_δ), 7.64 (s, 1H, H_μ), 7.68 (d, *J* = 5.0 Hz, 2H, β–pyridyl), 8.30 (d, *J* = 5.0 Hz, 2H, α–pyridyl), 9.17 (br, 1H, NH_{cis}); δ_C (100 MHz, $CDCl_3$) 12.5, 17.5, 23.2, 23.4, 25.7, 25.9, 26.7, 27.0, 27.3, 29.1, 30.6, 31.3, 32.4, 34.4, 34.5, 34.8, 35.9, 41.9, 45.6, 47.5, 49.9, 76.1, 78.4, 122.3, 126.3, 129.7, 130.9, 131.9, 132.3, 137.3, 142.0, 150.3, 164.3, 165.9, 176.6; ESI–MS: m/z 1251 $[M+H]^+$, 626 $[M+2H]^{2+}$.

Macrocycle 11

ν_{max}/cm^{-1} ($CDCl_3$) 1718, 1668; δ_H (400 MHz, $CDCl_3$) 0.88 (s, 3H, 18–Me), 0.97 (s, 3H, 19–Me), 1.03 (d, *J* = 6.4 Hz, 3H, 21–Me), 2.55 (m, 1H, 23–H), 2.69 (m, 1H, 23–H), 4.81 (m, 1H, 3βH), 5.48 (m, 1H, 12βH), 7.69 (m, 4H, $H_{\delta,\varepsilon}$), 7.86 (s, 1H, H_{μ}), 7.93 (d, *J* = 5.0 Hz, 2H, β–pyridyl), 8.75 (d, *J* = 5.0 Hz, 2H, α–pyridyl), 11.10 (br, 1H, NH_{cis}); δ_C (100 MHz, $CDCl_3$) 12.6, 18.1, 22.7, 25.6, 25.9, 26.1, 26.3, 27.5, 29.3, 30.6, 31.8, 31.9, 31.9, 33.7, 34.3, 34.6, 35.2, 35.5, 41.2, 45.3, 47.3, 49.9, 74.5, 77.7, 122.8, 126.9, 128.8, 129.6, 130.9, 138.1, 138.2, 143.4, 150.8, 164.1, 165.3, 178.4 ; ESI–MS: m/z 1877 $[M+H]^+$, 939 $[M+2H]^{2+}$.