Supplementary Material (ESI) for Organic & Biomolecular Chemistry

Supporting Information for:

Highly Diastereoselective Samarium Diiodide Induced Cyclizations of New 3-Substituted Indole Derivatives

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Contents

General Remarks:

Reactions were generally performed under argon in dried flasks. Solvents and reagents were added by syringes. Solvents were dried using standard procedures. Triethylamine and diisopropylamine were distilled from potassium hydroxide and stored over potassium hydroxide under an atmosphere of argon. Dichloromethane was distilled from calcium hydride and stored over molecular sieves (4 Å) under an atmosphere of argon. Methanol was distilled from magnesium oxide and stored over molecular sieves (4 Å) under an atmosphere of argon. Hexamethylphosphoramide (HMPA) was distilled from calcium hydride (130 °C, 12 mbar) and stored over molecular sieves (4 Å) under argon.

Warning: *HMPA has been identified as a carcinogenic reagent. Appropriate glove protection is required during handling. Reactions and chromatography should be performed in a well-vented hood.*

Other reagents were purchased and were used as received without further purification unless otherwise stated.

Products were purified by flash chromatography on silica gel (32-63 μm) or HPLC (Nucleosil 50–5, diameter 16 mm, length 244 mm) and detection was carried out with a Knauer variable UV-detector (λ =255 nm) and a Knauer refractometer. Unless otherwise stated, yields refer to analytically pure samples. Yields refer to chromatographically and spectroscopically (^{1}H-NMR) homogeneous materials, unless otherwise stated. Reactions were monitored by thin-layer chromatography (TLC). NMR spectra were recorded on Bruker (AM 250, AC 500) and JOEL (Eclipse 500) instruments. Chemical shifts are reported relative to TMS (^{1}H: δ = 0.00 ppm) and $CDCl_3$ (^{13}C: δ = 77.0 ppm). Integrals are in accordance with assignments; coupling constants are given in Hz. All ^{13}C spectra are proton-decoupled. Multiplicity is indicated as follows: s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), m_c (centered multiplet), dd (doublet of doublet), br s (broad singlet). For detailed peak assignments 2D spectra were measured (COSY, HMQC, HMBC, NOESY and NOE if necessary). IR spectra were measured with a Nicolet 5 SXC FT-IR spectrometer or with a Nexus FT-IR spectrometer equipped with a Nicolet Smart DuraSamplIR ATR. MS and HRMS analyses were performed with Finnigan MAT 711 (EI, 80 eV, 8 kV), MAT CH7A (EI, 80 eV, 3 kV) and Varian Ionspec QFT-7 (ESI-FT ICRMS) instruments. Elemental analyses were carried out with Vario EL III. Melting points were measured with a Reichert apparatus Thermovar and are uncorrected.

General Procedures:

General Procedure for Acylation Reaction

$SOCl_2$ (1.3 equiv.) was added dropwise to the corresponding acid (1.0 equiv.). The resulting solution was stirred for 2 h under exclusion of water. The excess of $SOCl_2$ was evaporated under reduced pressure. The obtained acid chloride was dissolved in CH_2Cl_2 and added to a mixture of indole derivative (0.8-0.6 equiv.), DMAP (0.10-0.05 equiv.) and TEA (1.3-1.1 equiv.) in CH_2Cl_2 (5 mL/1.0 mmol). The resulting mixture was stirred over night, then quenched with sat. aq. NH_4Cl solution and washed several time with water and brine. The organic phase was dried ($MgSO_4$), filtrated and the organic solvent evaporated under reduced pressure. The obtained residue was purified by column chromatography on silica gel.

General Procedure Samarium Diiodide Stock Solution:

SmI_2 was taken from a previously prepared stock solution (0.1 M in THF), which was prepared according to the following procedure: iodine (15.0 mmol, 1 equiv.) and samarium (18.0 mmol, 1.2 equiv.) were suspended in THF (150 mL, 10 mL/mmol I_2) under an argon atmosphere and stirred at room temperature until the colour of the solution turned into dark blue (1–5 h). The flask was then wrapped in aluminium foil to exclude light and stored at room temperature.

General Procedure for Samarium Diiodide-Induced Cyclizations with Proton Source:

To a solution of SmI_2 (2.4 equiv.) in THF was added HMPA (10.0 equiv.). The corresponding indole derivative (1.0 equiv.) and *t*BuOH (10.0 equiv.) were dissolved in THF (16 mL/mmol indole) and argon was bubbled through the solution for 10-20 min. The solution was added to the deep violet solution of SmI_2 in THF/HMPA. The mixture was stirred at room temperature for at least one hour (in most cases SmI_2 was consumed after a few minutes, the colour of the mixture turned from violet to yellow-grey). Sat. aq. $NaHCO_3$ solution was added, the organic layer was separated and the aq. layer was extracted three times with Et_2O. The combined organic layers were washed with water and brine, dried with $MgSO_4$ and the solvent was removed under reduced pressure. The crude product, which was contaminated with HMPA, was purified by flash-chromatography on silica gel and in singular cases additional purification by HLPC yielded the pure compounds.

General Procedure for Samarium Diiodide-Induced Cyclizations and Subsequent Alkylation:

To a solution of SmI_2 (2.4 equiv.) in THF was added HMPA (10.0 equiv.). The corresponding indole derivative (1.0 equiv.) and *t*BuOH (10.0 equiv.) were dissolved in THF (16 mL/mmol indole) and argon was bubbled through the solution for 10-20 min. The solution was added to the deep violet solution of SmI_2 in THF/HMPA. After the solution colour changed yellow-grew the alkylation reagent was added in one portion. The mixture was stirred at room temperature for at least one hour. Following work-up was done as stated above.

General Hydrogenation Procedure:

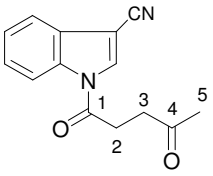
Hydrogen was bubbled either through a suspension washed Raney-Ni in MeOH (5-10 mL/mmol) for 2 h. Then a solution of the cyano compound in MeOH (3 mL/mmol) was added, and the mixture was stirred at room temperature under an atmosphere of hydrogen. Completion of the reaction was followed by TLC analysis. The solid residue was filtered off through a pad of silica gel and thoroughly washed with CH_2Cl_2/MeOH. The organic solvent was removed under reduced pressure, and the crude product was purified by column chromatography on silica gel.

General Alkylation Procedure with LDA

Freshly prepared LDA (0.5 M, THF) solution was added to indole derivative (5 mL THF/ 0.5 mmol indole) at -78 °C. After addition of HMPA (2.0-3.0 equiv) the solution was stirred at -78 °C for 20 min, then shortly warmed up to 0 °C and cooled to -78 °C again. Allyl iodide was added and the reaction was slowly warmed up to room temperature over night. The mixture was quenched with sat. aq. NH_4Cl and extracted three times with Et_2O. The combined organic phases were washed with water and brine, dried with $MgSO_4$ and evaporated. The crude mixture was purified by column chromatography on silica gel (hexane/EtOAc 9:1, 3:1).

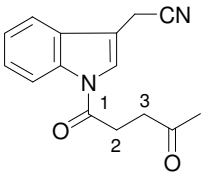
Characterization: Starting Material for Samarium Diiodide Induced Cyclization

1-(4-Oxopentanoyl)-1*H*-indole-3-carbonitrile (1)



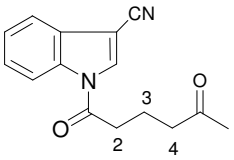
Yellow solid**:** 91%**;** 135-137 °C (Calcd for $C_{14}H_{12}N_2O_2$: C, 69.99; H, 5.03; N, 11.66%; found: C, 70.25; H, 5.17; N, 12.03%; ν_{max}/cm^{-1} = 3120-3070 (ArH), 2930 (CH), 2230 (CN), 1720, 1700 (CO), 1550 (CH); δ_H (400 MHz, $CDCl_3$, Me_4Si): 2.28 (3H, s, 5-H), 2.99 (2H, t, *J* = 5.9 Hz, 2-H), 3.21 (2H, t, *J* = 5.9 Hz, 3-H), 7.43 (2H, m_c, ArH), 7.70 (1H, d, *J* = 7.8 Hz, ArH), 8.11 (1H, s, ArH), 8.38 (1H, d, *J* = 7.8 Hz, ArH); δ_C (100 MHz, $CDCl_3$, Me_4Si): 29.6 (t, C-2), 29.9 (q, C-5), 37.1 (t, C-3), 94.2 (s, CN), 113.9 (s, Ar), 116.9, 119.7, 125.2, 127.1 (4d, Ar), 127.8 (s, Ar), 131.9 (d, Ar), 134.7, 170.0, 206.1 (3s, Ar, C-1, C-4); m/z (ESI-Tof): calcd for $C_{14}H_{12}N_2O_2$: 263.0791 $[M+Na]^+$; found 263.0800 $[M+Na]^+$).

2-(1-(4-Oxopentanoyl)-1*H*-indol-3-yl)acetonitrile (5)



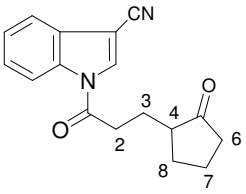
Colourless solid: 55%; 98-99 °C (Calcd for $C_{15}H_{14}N_2O_2$: C, 70.85; H, 5.55; N, 11.02%; found: C, 71.02; H, 5.72; N, 10.86%; ν_{max}/cm^{-1}: 3120-2900 (ArH, CH), 2250 (CN), 1785, 1710 (CO), 1565 (C=C); δ_H(400 MHz, $CDCl_3$, Me_4Si): 2.30 (3H, s, 5-H), 2.98 (2H, t, *J* = 6.0 Hz, 2-H), 3.22 (2H, t, *J* = 6.0 Hz, 3-H), 3.80 (2H, s, CH_2CN), 7.34 (1H, dd, *J* = 1.1, 7.6 Hz, ArH), 7.41 (1H, dt, *J* = 1.1, 7.6 Hz, ArH), 7.51 (1H, dd, *J* = 1.1, 7.6 Hz, ArH), 7.60 (1H, s, ArH), 8.42 (1H, d, *J* = 8.4 Hz, ArH); δ_C(100 MHz, $CDCl_3$, Me_4Si): 14.4 (t, CH_2CN), 29.5 (t, C-2), 29.9 (q, C-5), 37.1 (t, C-3), 111.6 (s, CN), 116.8, 118.0, 122.8, 123.9, 126.1 (5d, Ar), 128.3, 135.9 (2s, Ar), 169.9, 206.3 (2s, C-1, C-4)).

1-(5-Oxohexanoyl)-1*H*-indole-3-carbonitrile (9)



Colourless solid: 67%; 119-122 °C (Calcd for $C_{15}H_{14}N_2O_2$: C, 70.85; H, 5.55; N, 11.02%; found C, 70.50; H, 5.66; N, 11.03%; ν_{max}/cm^{-1}: 3110-3055 (ArH), 2990-2900 (CH), 2225 (CN), 1730, 1705 (CO), 1550 (C=C); δ_H (500 MHz, $CDCl_3$, Me_4Si): 2.11 (2H, t, *J* = 6.6 Hz, 3-H), 2.19 (3H, s, 6-H), 2.68 (2H, t, *J* = 6.6 Hz, 2-H), 3.01 (2H, t, *J* = 6.6 Hz, 4-H), 7.43 (1H, dd, *J* = 0.8, 7.8 Hz, ArH), 7.48 (1H, t, *J* = 7.8 Hz, ArH), 7.73 (1H, d, *J* = 7.8 Hz, ArH), 8.11 (s, 1H, ArH), 8.45 (1H, d, *J* = 8.3 Hz, ArH)**;** δ_C (100 MHz, $CDCl_3$, Me_4Si): 18.3 (t, C-3), 30.0 (q, C-6), 34.6, 41.7 (2t, C-4, C-2), 94.1 (s, CN), 116.9, 119.7, 125.1, 127.0 (4d, Ar), 127.8 (s, Ar), 131.8 (d, Ar), 134.6, 170.5, 207.8 (3s, Ar, C-1, C-5); m/z (ESI-Tof): calcd for $C_{15}H_{14}N_2O_2$: 277.0947 $[M+Na]^+$, found: 277.0949 $[M+Na]^+$).

1-(3-(2-Oxocyclopentyl)propanoyl)-1*H*-indole-3-carbonitrile (13)

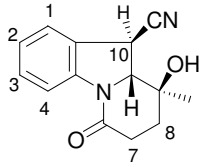


Colourless solid: 42%; 138-140 °C; (ν_{max}/cm^{-1}: 3120-3070 (ArH), 2960-2875 (CH), 2225 (CN), 1725 (br.s CO), 1555 (C=C); δ_H (400 MHz, $CDCl_3$, Me_4Si): 1.61 (1H, ddd, *J* = 5.1, 9.5, 17.0 Hz, 8-H), 1.85 (1H, m, 8-H), 1.98 (1H, td, *J* = 6.4, 14.3 Hz, 3-H), 2.00-2.40 (7H, m, 3-H, 4-H, 6-H, 7-H), 3.12 (1H, ddd, *J* = 6.4, 8.5, 16.6 Hz, 2-H), 3.21 (1H, ddd, *J* = 6.4, 8.5, 16.6 Hz, 2-H), 7.42 (1H, dt, *J* = 1.1, 7.6 Hz, ArH), 7.47 (1H, dt, *J* = 1.1, 7.6 Hz, ArH), 7.74 (1H, dd, *J* = 1.4, 7.6 Hz, ArH), 8.11 (1H, s, ArH), 8.45 (1H, d, *J* = 8.2 Hz, ArH); δ_C (100 MHz, $CDCl_3$, Me_4Si): 20.5, 24.4, 29.9, 33.2, 38.0 (5t, C-7, C-8, C-3, C-2, C-6), 47.5 (d, C-4), 94.0 (s, CN), 113.7, 116.9, 119.6, 125.1, 127.0 (4d, Ar), 127.9 (s, Ar), 131.9 (d, Ar), 134.7, 170.7, 220.7 (3s, Ar, C-1, C-5); m/z (ESI-Tof): calcd for $C_{17}H_{16}N_2O_2$: 303.1104 $[M+Na]^+$, found: 303.1132 $[M+Na]^+$).

Characterization:

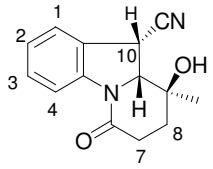
Products of Samarium Diiodide Induced Cyclization

rac-(9*S,9a*R**,10*R**)-9-Hydroxy-9-methyl-6-oxo-7,8,9,9a,10-hexahydropyrido[1,2-a]indole-10-carbonitrile (2)**



Colourless solid: 89%; 195-200 °C (Calcd for $C_{14}H_{14}N_2O_2$: C 69.41, H 5.82, N 11.56%; found C 69.04, H 5.12, N 11.48%; ν_{max}/cm^{-1}: 3270 (OH), 3070 (ArH), 2990-2985 (CH), 2250 (CN), 1630 (CO), 1480 (C=C); δ_H (500 MHz, $CDCl_3$+ 5% DMSO-d6, Me_4Si): 1.31 (3H, s, 9-CH_3), 2.01 (1H, ddd, *J* = 2.0, 7.9, 13.2 Hz, 8-H), 2.11 (1H, m_c, 8-H), 2.58 (1H, ddd *J* = 7.9, 11.5, 18.8 Hz, 7-H), 2.74 (1H, ddd, *J* = 2.0, 7.9, 18.8 Hz, 7-H), 4.39 (1H, d, *J* = 10.6 Hz, 10-H), 4.51 (1H, d, *J* = 10.6 Hz, 9a-H), 4.72 (1H, s, OH), 7.17 (1H, dt, *J* = 1.0, 7.6 Hz, 2-H), 7.34 (1H, t, *J* ~ 7.6 Hz, 3-H), 7.44 (1H, d, *J* = 7.6 Hz, 1-H), 8.18 (1H, d, *J* = 8.1 Hz, 4-H); δ_C (100 MHz, $CDCl_3$, Me_4Si): 19.5 (q, 9-CH_3), 30.9 (t, C-7), 33.1 (d, C-10), 35.6 (t, C-8), 68.9 (s, C-9), 71.1 (d, C-9a), 117.1 (d, C-4), 118.9 (s, CN), 124.0 (s, Ar), 124.2, 124.7, 129.7 (3d, C-1, C-3, C-2), 141.7, 167.2 (2s, Ar, C-6).; m/z (ESI-Tof): calcd for $C_{14}H_{14}N_2O_2$: 243.1134 $[M+H]^+$, 265.0948 $[M+Na]^+$; found 243.1137 $[M+H]^+$, 265.0958 $[M+Na]^+$).

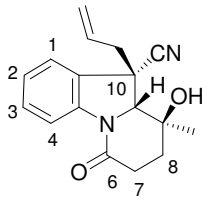
rac-(9*S,9a*R**,10*S**)-9-Hydroxy-9-methyl-6-oxo-7,8,9,9a,10-hexahydropyrido[1,2-a]indole-10-carbonitrile (3)**



Colorless solid: 22%; 135°C (ν_{max}/cm^{-1}: 3310 (OH), 3120 (ArH), 2990-2850 (CH), 2240 (CN), 1735 (CO), 1640 (CO), 1590 (C=C); δ_H (400 MHz, $CDCl_3$, Me_4Si): 1.67 (1H, s, 9-CH_3), 2.04 (2H, m_c, 8-H), 2.64 (1H, m_c, 7-H), 2.79 (1H, ddd, *J* = 4.5, 7.5, 18.1 Hz, 7-H), 4.41 (1H, d, *J* = 9.7 Hz, 9a-H), 4.51 (1H, d, *J* = 9.7 Hz, 10-H), 7.17 (1H, dt, *J* = 0.6, 7.6 Hz, 2-H), 7.37 (1H, t, *J* = 7.9 Hz, 3-H), 7.42 (1H, d, *J* = 7.5 Hz, 1-H), 8.23 (1H, d, *J* = 8.2 Hz, 4-H); δ_C (100 MHz, $CDCl_3$, Me_4Si): 21.0 (q, 9-CH_3), 30.9 (t, C-7), 32.6 (d, C-10), 37.3 (t, C-8), 67.0 (d, C-9a), 70.8 (s, C-9), 117.3 (s, CN), 117.8 (d, C-4), 123.6 (s, Ar), 124.8, 125.1, 130.4 (3d,

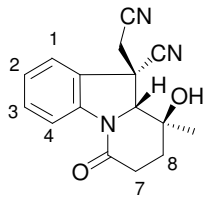
C-1, C-2, C-3), 142.3, 167.7 (2s, Ar, C-6); m/z (ESI-Tof): calcd for $C_{14}H_{14}N_2O_2$: 243.1134 $[M+H]^+$, 265.0948 $[M+Na]^+$; found 243.1139 $[M+H]^+$, 265.0956 $[M+Na]^+$).

rac-(9*S,9a*R**,10*S**)-10-Allyl-9-hydroxy-9-methyl-6-oxo-7,8,9,9a,10-hexahydropyrido[1,2-a]indole-10-carbonitrile (4, entry 1)**



Colourless solid: 48 %, based on recovered starting material; 120-123 °C (Calcd for $C_{17}H_{18}N_2O_2$: C 72.32, H 6.43, N 9.92%; found: C 71.85, H 6.19, N 9.80%; ν_{max}/cm^{-1}: 3460 (OH), 3115-3020 (ArH), 2975-2880 (CH), 2235 (CN), 1655 (CO), 1595 (C=C); δ_H (500 MHz, $CDCl_3$, Me_4Si): 1.50 (3H, s, 9-CH_3), 1.94 (1H, m_c, 8-H), 2.04 (1H, m, 8-H), 2.59 (1H, td, *J* = 8.2, 18.0 Hz, 7-H), 2.76 (1H, ddd, *J* = 4.6, 9.1, 18.0 Hz, 7-H), 2.82 (2H, m_c, 10-CH_2), 4.14 (1H, s, 9a-H), 5.25 (2H, m_c, CH=CH_2) 5.73 (1H, dddd, *J* = 6.6, 7.8, 10.2, 16.8 Hz, C*H*=CH_2), 7.15 (1H, dt, *J* = 1.1, 7.6 Hz, 2-H), 7.33 (1H, ddd, *J* = 1.3, 7.6, 8.2 Hz, 3-H), 7.39 (1H, ddd, *J* = 0.5, 1.2, 7.6 Hz, 1-H), 8.20 (1H, dd, *J* = 0.4, 8.2 Hz, 4-H); δ_C (100 MHz, $CDCl_3$, Me_4Si): 20. 7 (q, 9-CH_3), 31.0, 37.6, 44.4 (3t, C-7, C-8, 10-CH_2), 46.4 (s, C-10), 71.0 (d, C-9a), 71.3 (s, C-9), 116.7 (d, C-4), 120.3 (s, CN), 121.9 (t, CH=*C*H_2), 123.8, 124.8, 128.0 (3d, C-1, C-2, *C*H=CH_2), 130.1 (s, Ar), 130.3 (d, C-3), 141.5, 168.2 (2s, Ar, C-6); m/z (ESI-Tof): calcd for $C_{17}H_{18}N_2O_2$: 305.1266 $[M+Na]^+$, found: 305.1256 $[M+Na]^+$).

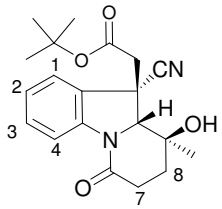
rac-(9*S,9a*R**,10*S**)-10-(Cyanomethyl)-9-hydroxy-9-methyl-6-oxo-7,8,9,9a,10-hexahydropyrido[1,2-a]indole-10-carbonitrile (4, entry 2)**



Colourless solid: 43%; 163-165 °C (Calcd for $C_{16}H_{15}N_3O_2$: C 68.31, H 5.37, N 14.94%; found: C 67.89, H 5.49, N 14.29%; ν_{max}/cm^{-1}: 3470 (OH), 3110-3010 (ArH), 2970-2855 (CH), 2270, 2240 (CN), 1665 (CO), 1600 (C=C); δ_H (500 MHz, $CDCl_3$, Me_4Si): 1.64 (1H, s, 9-CH_3), 1.97 (1H, ddd, *J* = 2.5, 7.7, 13.0 Hz, 8-H), 2.06 (1H, m_c, 8-H), 2.63 (1H, ddd, *J* = 7.8, 11.1, 18.7 Hz, 7-H), 2.74 (1H, ddd, *J* = 2.5, 7.7, 18.7 Hz, 7-H), 3.32 (1H, d, *J* = 16.8 Hz, 10-CH_2), 3.46 (1H, d, *J* = 16.8 Hz, 10-CH_2), 4.17 (1H, s, 9a-H), 4.36 (1H, s, OH), 7.23 (1H, dt, *J*

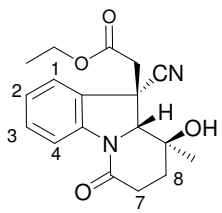
= 1.2, 7.7 Hz, 2-H), 7.41 (1H, dt, *J* = 1.2, 8.2 Hz, 3-H), 7.55 (1H, d, *J* = 7.7 Hz, 1-H), 8.28 (1H, d, *J* = 8.2 Hz, 4-H); δ_C (100 MHz, $CDCl_3$, Me_4Si): 19.9 (q, 9-CH_3), 28.9, 31.0, 38.3 (3t, 10-CH_2, C-7, C-8), 42.5 (s, C-10), 70.3 (s, C-9), 72.3 (d, C-9a), 114.7 (s, CN), 117.4 (d, C-4), 117.9 (s, CN), 123.2, 125.4 (2d, C-1, C-2), 125.9 (s, Ar), 131.4 (d, C-3), 141.8, 167.4 (2s, Ar, C-6); m/z (ESI-Tof): calcd for $C_{16}H_{15}N_3O_2$: 304.1057 $[M+Na]^+$, 320.0801 $[M+K]^+$, found: 304.1077 $[M+Na]^+$, 320.0794 $[M+K]^+$).

rac-*(9S*,9aR*,10S*)*-*tert*-Butyl-2-(10-cyano-9-hydroxy-9-methyl-6-oxo-7,8,9,9a,10-hexahydropyrido[1,2-a]indol-10-yl)acetate (4, entry 3)



Yellow oil: 32% (ν_{max}/cm^{-1}: 3430 (OH), 3180-3070 (ArH), 2975-2930 (CH), 2240 (CN), 1725 (CO), 1665-1645 (CO), 1595 (C=C); δ_H (500 MHz, $CDCl_3$, Me_4Si): 1.39 (9H, s, $C(CH_3)_3$), 1.55 (3H, s, 9-CH_3), 1.99 (1H, ddd, *J* = 4.1, 8.2, 13.3 Hz, 8-H), 2.05 (1H, dtd, *J* = 0.7, 8.8, 13.3 Hz, 8-H), 2.62 (1H, m_c, 7-H), 2.77 (1H, ddd, *J* = 4.2, 8.6, 18.1 Hz, 7-H), 2.99 (1H, d, *J* = 15.8 Hz, 10-CH_2), 3.16 (1H, d, *J* = 15.8 Hz, 10-CH_2), 3.29 (1H, br.s, OH), 4.47 (1H, s, 9a-H), 7.17 (1H, dt, *J* = 1.0, 7.7 Hz, 2-H), 7.36 (1H, dt, *J* = 1.3, 8.2 Hz, 3-H), 7.42 (1H, dd, *J* = 0.7, 7.7 Hz, 1-H), 8.24 (1H, dd, *J* = 0.4, 8.2 Hz, 4-H); δ_C (125 MHz, $CDCl_3$, Me_4Si): 20.5 (q, 9-CH_3), 27.8 (q, $C(CH_3)_3$), 30.8, 37.7, 42.4 (3t, C-7, C-8, 10-CH_2), 45.9 (s, C-10), 71.1 (s, C-9), 72.5 (d, C-9a), 83.4 (s, $CO_2C(CH_3)_3$), 116.9 (d, C-4), 119.2 (s, CN), 123.5, 124.8 (2d, C-1, C-2), 127.5 (s, Ar), 130.6 (d, C-3), 141.5, 168.0, 168.3 (3s, Ar, C-6, $CO_2C(CH_3)_3$); m/z (ESI-Tof): calcd for $C_{20}H_{24}N_2O_4$: 357.1814 $[M+H]^+$, 379.1634 $[M+Na]^+$, 395.1373 $[M+K]^+$, found: 357.1824 $[M+H]^+$, 379.1643 $[M+Na]^+$, 395.1386 $[M+K]^+$).

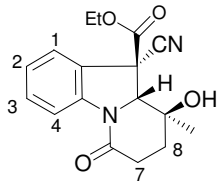
rac-((9S*,9aR*,10R*)- Ethyl (10-cyano-9-hydroxy-9-methyl-6-oxo-7,8,9,9a,10-hexahydropyrido[1,2-a]indol-10-yl)acetate (4, entry 4)



Yellow oil: 41%; based on recovered starting material (ν_{max}/cm^{-1}: 3430 (OH), 3185-3070 (ArH), 2985-2935 (CH), 2240 (CN), 1720 (CO), 1670-1645 (CO), 1595 (C=C); δ_H (700 MHz,

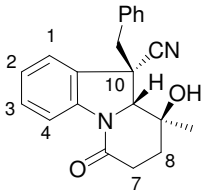
$CDCl_3$, Me_4Si): 1.19 (2H, t, J = 7.16 Hz, CH_2CH_3), 1.55 (3H, s, 9-CH_3), 1.96 (1H, ddd, J = 3.8, 8.2, 13.3 Hz, 1H, 8-H), 2.03 (1H, td, J = 9.3, 13.3 Hz, 8-H), 2.68-2.55 (1H, m_c, 7-H), 2.74 (1H, ddd, J = 3.8, 8.6, 18.1, Hz, 7-H), 3.08 (1H, d, J = 16.2 Hz, 10-CH_2), 3.23 (1H, d, J = 16.2 Hz, 10-CH_2), 3.46 (1H, s, 9a-H), 4.25-4.09 (2H, m, CH_2CH_3), 4.43 (1H, s, 9a-H), 7.15 (1H, dt, J = 1.1, 7.6 Hz, 1-H), 7.35 (1H, ddd, J = 1.3, 7.6, 8.2 Hz, 3-H), 7.41 (1H, dd, J = 0.8, 7.6 Hz, 2-H), 8.22 (1H, d, J = 8.2 Hz, 4-H); δ_C (100 MHz, $CDCl_3$, Me_4Si): 13.9 (q, CH_2CH_3), 20.3 (q, 9-CH_3), 30.8, 37.8 (2t, C-7, C-8), 42.3 (s, C-10), 44.5 (t, 10-CH_2), 61.8 (t, CH_2CH_3), 72. 5 (d, C-9a), 80.0 (s, C-9), 116.9 (d, C-4), 119.1 (s, CN), 123.4, 124.9 (2d, C-2, C-3), 127.5 (s, Ar), 130.6 (d, C-1), 141.5, 168.1, 169.0 (3s, Ar, C-6, CO_2Et); m/z (ESI-Tof): calcd for $C_{18}H_{20}N_2O_4$: 351.1315 $[M+Na]^+$, found: 351.1328 $[M+Na]^+$).

rac-(9*S,9a*R**,10*R**)-10-Cyano-9-hydroxy-9-methyl-6-oxo-7,8,9,9a,10-hexahydro-pyrido-[1,2-a]indole-10-carboxylic acid ethyl ester (4, entry 5)**



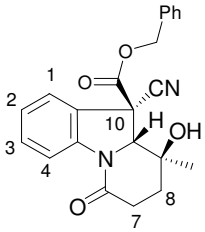
Yellow oil: 67% (ν_{max}/cm^{-1}: 3400 (OH), 3120-3075 (ArH), 2980-2940 (CH), 2245 (CN), 1745 (CO), 1660, 1645 (CO), 1590 (C=C); δ_H (500 MHz, $CDCl_3$, Me_4Si): 1.39 (3H, t, J = 14.3 Hz, CH_2CH_3), 1.63 (3H, s, 9-CH_3), 2.02 (2H, m_c, 8-H), 2.63 (1H, m_c, 7-H), 2.81 (1H, ddd, J = 4.1, 7.3, 18.4 Hz, 7-H), 2.97 (1H, s, OH), 4.39 (2H, ddd, J = 7.1, 14.2, 14.3 Hz, CH_2CH_3), 4.97 (1H, s, 9a-H), 7.16 (1H, dt, J = 1.0, 7.7 Hz, 2-H), 7.39 (1H, dt, J = 1.3, 8.0 Hz, 3-H), 7.43 (1H, dd, J = 0.7, 7.7 Hz, 1-H), 8.22 (1H, d, J = 8.0 Hz, 4-H); δ_C (100 MHz, $CDCl_3$, Me_4Si): 13.9 (q, CH_2CH_3), 20.5 (q, 9-CH_3), 30.8, 37.5 (2t, C-7, C-8), 50.9, 64.4 (2t, CH_2CH_3), 70.2 (s, C-9), 71.5 (d, C-9a), 116.2 (s, CN), 117.6 (d, C-4), 123.7 (d, C-1), 125.0 (s, Ar), 125.3, 131.2 (d, C-2, C-3), 141.7, 166.2, 167.8 (3s, Ar, C-6, CO_2Et); m/z (ESI-Tof): calcd for $C_{17}H_{18}N_2O_4$: 315.1339 $[M+H]^+$, 337.1159 $[M+Na]^+$, found: 315.1369 $[M+H]^+$, 337.1189 $[M+Na]^+$).

rac-(9*S,9a*R**,10*S**)-10-Benzyl-9-hydroxy-9-methyl-6-oxo-7,8,9,9a,10-hexahydropyrido[1,2-a]indole-10-carbonitrile (4, entry 6)**



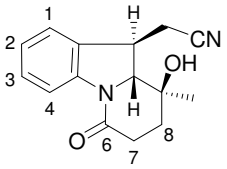
Colourless oil: 35% (ν_{max}/cm^{-1}: 3390 (OH), 3085-3030 (ArH), 2925-2850 (CH), 2235 (CN), 1640 (CO), 1595 (C=C); δ_H (400 MHz, $CDCl_3$, Me_4Si): 1.46 (3H, s, 9-CH_3), 1.92 (1H, ddd, *J* = 5.1, 8.4, 13.5 Hz, 8-H), 2.00 (1H, m_c, 8-H), 2.56 (1H, ddd, *J* = 7.5, 8.4, 17.7 Hz, 7-H), 2.72 (1H, ddd, *J* = 5.1, 9.3, 17.7 Hz, 7-H), 3.26 (1H, d, *J* = 13.5 Hz, 10-CH_2), 3.45 (1H, d, *J* = 13.5 Hz, 10-CH_2), 4.23 (1H, s, 9a-H), 7.06 (1H, dd, *J* = 1.3, 7.6 Hz, 1-H), 7.10 (3H, m_c, Ph), 7.28 (3H, m_c, 2-H, Ph), 7.33 (1H, m_c, 3-H), 8.16 (1H, d, *J* = 8.2 Hz, 4-H); δ_C (100 MHz, $CDCl_3$, Me_4Si): 21.0 (q, 9-CH_3), 30.8, 37.3 (2t, C-7, C-8) 45.8 (s, C-10), 48.1 (t, 10-CH_2), 71.1 (d, C-9a), 71.5 (s, C-9), 116.5 (d, Ar), 120.5 (s, Ar), 124.3, 124.6 (2d, Ar), 127.6 (s, Ar), 128.0, 128.4, 130.3, 130.9 (4d, Ar), 133.1, 141.5, 168.2 (3s, Ph, Ar, C-6); m/z (ESI-Tof): calcd $C_{21}H_{20}N_2O_2$: 355.1417 $[M+Na]^+$, found 355.1429 $[M+Na]^+$).

rac-(9*S,9a*R**,10*R**)-Benzyl 10-Cyano-9-hydroxy-9-methyl-6-oxo-7,8,9,9a,10-hexahydropyrido[1,2-a]indole-10-carboxylate (4, entry 7)**



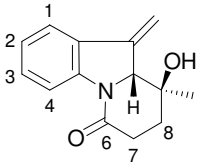
Colourless oil: 61% (ν_{max}/cm^{-1}: 3390 (OH), 3090-3030 (ArH), 2970-2890 (CH), 2245 (CN), 1750 (CO), 1645 (CO), 1590 (C=C); δ_H (500 MHz, $CDCl_3$, Me_4Si): 1.62 (3H, s, 9-CH_3), 2.04 (2H, m_c, 8-H), 2.64 (1H, m_c, 7-H), 2.81 (1H, ddd, *J* = 4.9, 6.9, 18.3 Hz, 7-H), 4.96 (1H, s, 9a-H), 5.33 (1H, d, *J* = 12.1 Hz, C*H*$_2$Bn), 5.40 (1H, d, *J* = 12.1 Hz, C*H*$_2$Bn), 7.09 (1H, dt, *J* = 0.9, 7.6 Hz, 2-H), 7.31 (1H, dd, *J* = 0.7, 7.8 Hz, 1-H), 7.38 (6H, m_c, Ph, 3-H), 8.22 (1H, dd, *J* = 0.5, 8.2 Hz, 4-H); δ_C (100 MHz, $CDCl_3$, Me_4Si): 20.6 (q, 9-CH_3), 30.7, 37.5 (2t, C-7, C-8), 51.0 (s, C-10), 69.7 (t, *C*H_2Bn), 70.4 (s, C-9), 71.4 (d, C-9a), 116.0 (s, CN), 117.5 (d, C-4), 123.9 (d, C-1) 124.6 (s, Ar), 125.2, 128.3, 128.7, 128.9, 131.3 (5d, C-2, Ph, C-3), 134.0, 141.7, 166.0, 167.5 (4s, Ar, 10-*C*O_2Bn, C-6); m/z (ESI-Tof): calcd $C_{22}H_{20}N_2O_4$: 377.1496 $[M+H]^+$, 399.1315 $[M+Na]^+$, 415.1055 $[M+K]^+$; found: 377.1495 $[M+H]^+$, 399.1313 $[M+Na]^+$, 415.1051 $[M+K]^+$).

rac-(9*S, 9a*R**,10*S**)-9-Hydroxy-9-methyl-6-oxo-7,8,9,9a,10-hexahydropyrido[1,2-*a*]indole-10-yl-acetonitrile (6)**



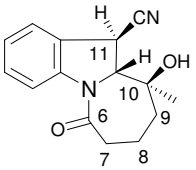
Colourless solid: 90%; 193-194 °C (Calcd for $C_{15}H_{16}N_2O_2$: C 70.29, H 6.29, N 10.93%; found C 70.01, H 6.34, N 10.87%; ν_{max}/cm^{-1}: 3210 (OH), 3045 (ArH), 2965-2900 (CH), 2245 (CN), 1635 (CO), 1600-1590 (C=C); δ_H (400 MHz, $CDCl_3$, Me_4Si): 1.33 (3H, s, 9-CH_3), 1.86 (1H, s, OH), 1.99 (1H, ddd, *J* = 2.5, 7.9, 13.0 Hz, 8-H), 2.07 (1H, m_c, 8-H), 2.59 (1H, ddd, *J* = 8.0, 11.3, 18.5 Hz, 7-H), 2.75 (1H, ddd, *J* = 2.5, 8.0 18.5 Hz, 7-H), 2.93 (1H, dd, *J* = 6.5, 17.0 Hz, 10-CH_2), 3.09 (1H, dd, *J* = 4.3, 17.0 Hz, 10-CH_2), 3.74 (1H, m_c, 10-H), 4.00 (1H, d, *J* = 9.7 Hz, 9a-H), 7.14 (1H, dd, *J* = 1.0, 7.5 Hz, 2-H), 7.31 (1H, t, *J* = 7.8 Hz, 3-H), 7.39 (1H, d, *J* = 7.5 Hz, 1-H), 8.20 (1H, d, *J* = 8.1 Hz, 4-H); δ_C (100 MHz, $CDCl_3$, Me_4Si): 20.6 (q, 9-CH_3), 21.6, 31.0, 37.0 (3t, C-7, C-8, 10-*C*H_2CN), 38.8 (d, C-10), 70.6 (s, C-9), 71.4 (d, C-9a), 117.1 (d, C-4), 117.9 (s, CN), 123.2, 124.8, 129.2 (3d, C-1, C-2, C-3), 129.7, 142.0 (2s, Ar), 167.1 (s, C-6)).

rac-(9*S,9a*R**)-9-Hydroxy-9-methyl-10-methylene-8,9,9a,10-tetrahydropyrido[1,2-*a*]indol-6(7*H*)-one (8)**



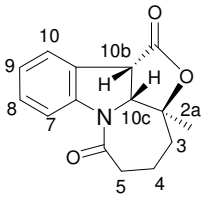
Colourless oil: 60% (ν_{max}/cm^{-1}: 3370 (OH), 3120-3050 (ArH), 2970-2855 (CH, C=CH_2), 1635 (CO), 1595 (C=C); δ_H (400 MHz, $CDCl_3$, Me_4Si): 1.17 (3H, s, 9-CH_3), 2.01 (1H, ddd, *J* = 4.1, 7.7, 13.7 Hz, 8-H), 2.12 (1H, ddd, *J* = 7.7, 8.8, 13.7 Hz, 8-H), 2.60 (1H, m_c, 7-H), 2.78 (1H, ddd, *J* = 6.2, 8.8, 17.4 Hz, 7-H), 4.68 (1H, t, *J* = 2.8 Hz, 9a-H), 5.44 (1H, d, *J* = 2.6 Hz, 10-CH_2), 5.64 (1H, d, *J* = 2.6 Hz, 10-CH_2), 7.09 (1H, t, *J* = 7.6 Hz, 2-H), 7.29 (1H, d, *J* = 8.6 Hz, 3-H), 7.49 (1H, d, *J* = 7.6 Hz, 1-H), 8.22 (1H, d, *J* = 8.6 Hz, 4-H); δ_C (100 MHz, $CDCl_3$, Me_4Si): 21.4 (q, 9-CH_3), 31.0, 36.5 (2t, C-7, C-8), 68.7 (d, C-9a), 72.1 (s, C-9), 104.2 (t, =CH_2), 116.9, 120.1, 124.1 (3d, C-4, C-1, C-2), 128.9 (s, Ar), 130.1 (d, C-3), 141.7, 143.7 (2s, Ar), 168.0 (s, C-6); m/z (ESI-Tof): calcd for $C_{14}H_{15}NO_2$: 230.1176 $[M+H]^+$, 252.0995 $[M+Na]^+$, found 230.1177 $[M+H]^+$, 252.0996 $[M+Na]^+$).

rac-(9*S,9a*R**,10*R**)-10-Hydroxy-10-methyl-6-oxo-7,8,9,10,10a,11-hexahydro-6*H*-azepino[1,2-a]indole-11-carbonitrile (10)**



Colourless solid: 42%; 198-200 °C (for $C_{15}H_{16}N_2O_2$: C 70.29, H 6.29, N 10.93%; found C 69.98, H 6.31, N 10.84%; ν_{max}/cm^{-1}: 3315 (OH), 3125-3035 (ArH), 2995-2865 (CH), 2240 (CN), 1635 (CO), 1595 (C=C); δ_H (400 MHz, $CDCl_3$, Me_4Si): 0.89 (3H, s, 10-CH_3), 1.70 (1H, dddd, *J* = 1.7, 3.7, 11.3, 14.0 Hz, 8-H), 1.87 (1H, dt, *J* = 3.5, 13.1 Hz, 9-H), 1.95 (1H, m_c, 8-H), 2.04 (1H, dt, *J* = 3.4, 13.1 Hz, 9-H), 2.64 (2H, m_c, 7-H), 4.62 (1H, d, *J* = 3.9 Hz, 10a-H), 4.76 (1H, d, *J* = 3.9 Hz, 11-H), 7.09 (1H, t, *J* = 7.5 Hz, 2-H), 7.29 (1H, t, *J* = 7.5 Hz, 3-H), 7.33 (1H, d, *J* = 7.5 Hz, 1-H), 8.17 (1H, d, *J* = 8.3 Hz, 4-H); δ_C(100 MHz, $CDCl_3$, Me_4Si): 18.6 (q, 10-CH_3), 20.3 (t, C-9), 32.6 (d, C-11), 38.5, 45.1 (2t, C-8, C-7), 71.3 (d, C-10a), 71.6 (s, C-10), 117.6 (d, C-4), 119.9 (s, CN), 124.1 (s, Ar), 124.5, 124.9, 130.0 (3d, C-1, C-2, C-3), 142.8, 172.4 (2s, Ar, C-6); m/z (ESI-Tof): calcd for $C_{15}H_{16}N_2O_2$: 257.1285 $[M+H]^+$, 279.1104 $[M+Na]^+$, 295.0843 $[M+K]^+$, found: 257.1292 $[M+H]^+$, 279.1112 $[M+Na]^+$, 295.0853 $[M+K]^+$).

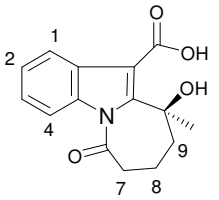
rac-(2a*S,10b*S**,10c*R**)-2a-Methyl-2a,3,4,5,10b,10c-hexahydro-2-oxa-6a-azabenzo[*a*]cyclopenta[*cd*]azulene-1,6-dione (11)**



Colourless solid: 39%; 157-160 °C (for $C_{15}H_{15}NO_3$: C 70.02, H 5.88, N 5.44%; found C 69.52, H 5.77, N 5.89%; ν_{max}/cm^{-1}: 3105-3050 (ArH), 3000-2855 (CH), 1775 (CO), 1670 (CO), 1595 (C=C); δ_H (500 MHz, $CDCl_3$, Me_4Si): 1.02 (3H, s, 2a-CH_3), 1.25 (1H, br.s, OH), 1.92 (1H, m_c, 4-H), 2.04 (1H, m_c, 3-H), 2.11 (1H, m_c, 4-H), 2.21 (1H, ddd, *J* = 2.4, 4.1, 12.1 Hz, 3-H), 2.70 (1H, ddd, *J* = 2.2, 5.6, 14.3 Hz, 5-H), 2.93 (1H, dt, *J* = 2.9, 13.9 Hz, 5-H), 4.47 (1H, d, *J* = 10.3 Hz, 10b-H), 4.88 (1H, d, *J* = 10.3 Hz, 10c-H), 7.14 (1H, dt, *J* = 0.8, 7.5 Hz, 9-H), 7.34 (1H, t, *J* = 7.8 Hz, 8-H), 7.49 (1H, d, *J* = 7.6 Hz, 10-H), 8.10 (1H, d, *J* = 8.1 Hz, 7-H); δ_C (100 MHz, $CDCl_3$, Me_4Si): 19.9 (q, 2a-CH_3), 20.7, 38.4, 38.6 (3t, C-3, C-4, C-5) 46.6, 67.0 (2d, C-10b, C-10c), 86.4 (s, C-2a), 116.3 (d, C-7), 124.6 (s, Ar), 124.8, 124.8, 129.6 (3d, C-10, C-9, C-8), 143.0, 171.4, 172.9 (3s, Ar, C-6, C-1); m/z (ESI-Tof): Calcd for

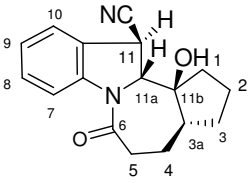
$C_{15}H_{15}NO_3$: 258.11247 $[M+H]^+$, 280.0944 $[M+Na]^+$; found: 258.1130 $[M+H]^+$, 280.0950 $[M+Na]^+$).

rac-(10*S)-10-Hydroxy-10-methyl-6-oxo-7,8,9,10-tetrahydro-6*H*-azepino[1,2-a]indole-11-carboxylic acid (12)**



Colourless solid: 7%, (ν_{max} /cm^{-1}: 3400 (OH), 3100-3030 (ArH), 3005-2850 (CH), 1775 (CO), 1700 (CO), 1595 (C=C); δ_H (500 MHz, $CDCl_3$, Me_4Si): 0.90 (3H, s, 10-CH_3), 1.89 (1H, m_c, 8-H), 2.09 (2H, m_c, 8-H, 9-H), 2.21 (1H, m_c, 9-H), 2.68 (1H, ddd, *J* = 2.5, 5.7, 14.5 Hz, 7-H), 2.94 (1H, dt, *J* = 2.7, 14.0 Hz, 7-H), 4.65 (1H, s, OH), 4.77 (1H, s, CO_2H), 7.20 (1H, dt, J = 0.9, 7.5 Hz, 2-H), 7.45 (dt, 1H, *J* = 1.3, 7.9 Hz, 3-H), 7.60 (1H, dd, *J* = 0.7, 7.6 Hz, 1-H), 8.14 (d, 1H, *J* = 8.2 Hz, 4-H); δ_C (100 MHz, $CDCl_3$ + 10% d_6-Aceton, Me_4Si): 19.6 (q, 10-CH_3), 20.8, 38.2, 39.1 (3t, C-9, C-8, C-7), 74.4, 79.8, 82.9 (3s, C-10, C-10a, C-11), 116.4, 124.8, 124.9 (3d, C-4, C-3, C-2), 128.8 (s, Ar), 131.5 (d, C-1), 143.7, 171.6, 173.8 (3s, Ar, C-6, 11-CO_2H); m/z (ESI-Tof): Calcd for $C_{15}H_{15}NO_4$: 296.0893 $[M+Na]^+$, 569.1894 $[2M+Na]^+$, found 296.0884 $[M+Na]^+$, 569.1911 $[2M+Na]^+$).

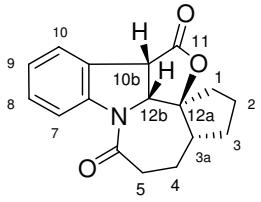
rac-(3a*R,11*R**,11a*R**,11b*S**)-11b-Hydroxy-6-oxo-1,2,3,3a,4,5,6,11,11a,11b-decahydrocyclopenta[3,4]azepino[1,2-*a*]indole-11-carbonitrile (14)**



Colourless solid: 41%; 182-183 °C (Calcd for $C_{17}H_{18}N_2O_3$: C 72.32, H 6.43, N 9.92%; found C, 72.35, H 5.58, N 9.81%); ν_{max}/cm^{-1}: 3310 (OH), 3120-3025 (ArH), 2970-2870 (CH), 2235 (CN), 1650 (br.s CO), 1595 (C=C); δ_H (500 MHz, $CDCl_3$, Me_4Si): 1.33 (1H, m_c, 3-H), 1.39 (1H, ddd, *J* = 3.1, 9.5, 12.6 Hz, 1-H), 1.50 (2H, m_c, 4-H, 3-H), 1.75 (2H, m_c, 2-H), 1.91 (1H, ddd *J* = 2.9, 6.3, 14.6 Hz, 4-H), 2.11 (1H, td, *J* = 6.1, 12.4 Hz, 1-H), 2.20 (1H, m_c, 3a-H), 2.61 (1H, dd, *J* = 7.6, 14.0 Hz, 5-H), 2.76 (1H, t, *J* = 13.1 Hz, 5-H), 3.01 (s, 1H, OH), 4.71 (1H, d, 1H, *J* = 4.1 Hz, 11a-H), 4.95 (1H, d, *J* = 4.1 Hz, 11-H), 7.13 (1H, dt, *J* = 0.9, 7.6 Hz, 9-H), 7.33 (1H, t, *J* = 7.9 Hz, 8-H), 7.36 (1H, d, *J* = 7.6 Hz, 10-H), 8.19 (1H, d, *J* = 8.2 Hz, 7-H); δ_C

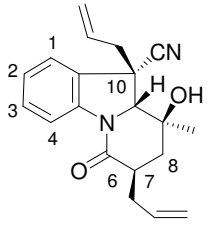
(100 MHz, $CDCl_3$, Me_4Si): 19.7, 27.2, 27.3, 30.3 (4t, C-2, C-4, C-3, C-1), 33.5 (d, C-11), 36.5 (t, C-5), 52.0, 68.0 (2d, C-3a, C-11a), 82.4 (s, C-11b), 117.6 (d, C-7), 119.8, 123.8 (2s, CN, Ar), 124.5, 124.6, 129.9 (3d, C-10, C-9, C-8), 142.5, 172.8 (2s, Ar)).

rac-(3a*R,10b*S**,12a*S**,12b*R**)-1,2,3,3a,4,5,10b,12b-Octahydro-6*H*,11*H*-12-oxa-6a-azabenzo[*a*]dicyclopenta[*cd*,*e*]azulene-6,11-dione (15)**



Colourless solid: 40%; decomposition > 110 °C (Calcd for $C_{17}H_{17}NO_3$: C, 72.07; H, 6.05; N, 4.94%; found: C, 71.85; H, 6.14; N, 5.15%; ν_{max}/cm^{-1}: 3070-3050 (ArH), 2975-2875 (CH), 1770 (br.s. CO), 1660 (CO), 1595 (C=C); δ_H(400 MHz, $CDCl_3$, Me_4Si): 1.08 (1H, m_c, 3-H), 1.47 (3H, m_c, 3-H, 2-H), 1.60 (1H, s, OH), 1.76 (2H, m_c, 1-H), 2.02 (2H, m_c, 4-H, 3-H), 2.36 (1H, m_c, 3a-H), 2.58 (1H, ddd, *J* = 2.2, 6.2, 14.1 Hz, 5-H), 3.02 (1H, dt, *J* = 2.6, 14.1 Hz, 5-H), 4.43 (1H, d, *J* = 9.8 Hz, 10b-H), 5.18 (1H, d, *J* = 9.8 Hz, 12b-H), 7.14 (1H, dt, *J* = 1.0, 7.5 Hz, 9-H), 7.34 (1H, m_c, 8-H), 7.47 (1H, d, *J* = 7.6 Hz, 10-H), 8.10 (1H, d, *J* = 8.1 Hz, 7-H); δ_C (100 MHz, $CDCl_3$, Me_4Si): 19.3, 27.9, 28.7, 29.8, 37.3 (5t, C-4, C-3, C-2, C-1, C-5), 46.1, 47.4, 62.8 (3d, C-3a, C-10b, C-12b), 96.4 (s, C-12a), 116.6 (d, C-7), 124.4 (s, Ar), 125.1, 125.1, 129.8 (3d, C-10, C-9, C-8), 142.5 (s, Ar), 171.6, 172.9 (2s, C-6, C-11); m/z (ESI-Tof): Calcd for $C_{17}H_{17}NO_3$: 284.1281 $[M+H]^+$, 306.1101 $[M+Na]^+$, found: 284.1278 $[M+H]^+$, 306.1098 $[M+Na]^+$).

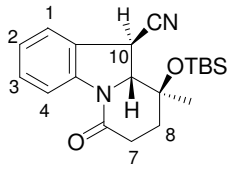
rac-(7*R,9*S**,9a*R**,10*S**)-7,10-Diallyl-9-hydroxy-9-methyl-6-oxo-7,8,9,9a,10-hexahydropyrido[1,2-a]indole-10-carbonitrile (17)**



Colourless oil: 83 % (ν_{max}/cm^{-1}: 3075-3060 (ArH), 2990-2870 (CH), 1770 (CO), 1620, 1595 (C=C); δ_H(400 MHz, $CDCl_3$, Me_4Si): 1.57 (s, 3H, 9-CH_3), 1.78 (1H, ddd, *J* = 1.0, 10.5, 13.0 Hz, 8-H), 2.03 (1H, dd, *J* = 8.2, 13.0 Hz, 8-H), 2.26 (1H, s, OH), 2.51 (1H, dddd, *J* = 1.0, 2.1, 7.3, 13.8 Hz, 7-CH_2), 2.66 (1H, m_c, 7-CH_2), 2.74 (1H, dtd, *J* = 4.0, 8.3, 10.5 Hz, 7-H), 2.85 (1H, dd, *J* = 8.3, 14.0 Hz, 10-CH_2), 2.92 (1H, tdd, *J* = 1.4, 6.2, 14.0 Hz, 10-CH_2), 5.12 (1H,

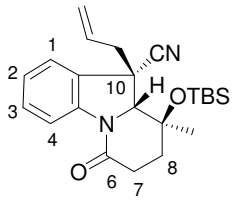
tdd, *J* = 1.0, 2.0, 10.1 Hz, CH=C*H*$_2$), 5.18 (1H, m$_c$, CH=C*H*$_2$), 5.26 (1H, ddd, *J* = 1.6, 2.7, 17.0 Hz, CH=C*H*$_2$), 5.29 (1H, ddd, *J* = 1.0, 2.2, 10.1 Hz, CH=C*H*$_2$), 5.77 (2H, m$_c$, C*H*=CH$_2$), 7.17 (1H, dt, *J* = 1.1, 7.6 Hz, 2-H), 7.35 (1H, ddd, *J* = 1.3, 7.6, 8.2 Hz, 3-H), 7.40 (1H, ddd, *J* = 0.6, 1.3, 7.6 Hz, 1-H), 8.28 (1H, ddd, *J* = 0.6, 1.1, 8.2 Hz, 4-H); δ_C (100 MHz, $CDCl_3$, Me_4Si): 20.1 (q, 9-CH_3), 37.2 (t, C-8), 40.9 (d, C-7), 43.9 (t, 10-CH_2), 44.3 (s, C-10), 46.6 (t, 7-CH_2), 71.0 (s, C-9), 71.2 (d, C-9a), 117.1 (d, C-4), 118.5 (t, =CH_2), 120.5 (s, CN), 121.9 (t, =CH_2), 123.8, 125.0 (2d, C-1, C-3), 127.9 (s, Ar), 130.4 (d, C-2), 130.5, 134.4 (2d, C*H*=CH$_2$), 141.9, 169.7 (2s, Ar, C-6); m/z (ESI-Tof): Calcd for $C_{20}H_{22}N_2O_2$: 323.1754 $[M+H]^+$, 345.1573 $[M+Na]^+$; found: 323.1757 $[M+H]^+$, 345.1579 $[M+Na]^+$).

rac-(9*S,9a*R**,10*R**)-9-(*tert*-Butyl-dimethylsilyloxy)-9-methyl-6-oxo-7,8,9,9a,10-hexahydropyrido[1,2-a]indole-10-carbonitrile (18)**



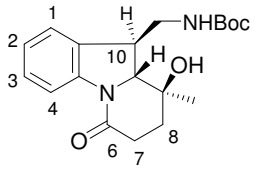
Colourless solid: 95%, 115-118 °C (Calcd for $C_{20}H_{28}N_2O_2Si$: C 67.37, H 7.92, N 7.86%; found C 67.35, H 8.02, N 7.76%; ν_{max}/cm^{-1}: 2965-2855 (ArH, CH), 2245 (CN), 1660, 1650 (CO), 1600 (C=C); δ_H (500 MHz, $CDCl_3$, Me_4Si): 0.20 (3H, s, $SiCH_3$), 0.21 (3H, s, $SiCH_3$), 0.95 (9H, s, $SiC(CH_3)_3$), 1.33 (3H, s, 9-CH_3), 2.09 (1H, dd, *J* = 9.2, 4.4 Hz, 8-H), 2.54 (1H, td, *J* = 9.4, 18.9 Hz, 7-H), 2.76 (1H, ddd, *J* = 5.7, 4.2, 18.6 Hz, 7-H), 4.31 (1H, d, *J* = 10.2 Hz, 10-H), 4.44 (1H, d, *J* = 10.2 Hz, 9a-H), 7.15 (1H, t, *J* = 7.5 Hz, 2-H), 7.32 (1H, t, *J* = 7.8 Hz, 3-H), 7.42 (1H, d, *J* = 7.5 Hz, 1-H), 8.16 (1H, d, *J* = 8.1 Hz, 4-H); δ_C (100 MHz, $CDCl_3$, Me_4Si): -1.9, -1.8 (2q, $SiCH_3$), 17.9 (s, $SiC(CH_3)_3$), 20.4 (q, 9-CH_3), 25.6 (q, $C(CH_3)_3$), 30.8 (t, C-8), 33.2 (d, C-10), 36.0 (t, C-7), 71.7 (d, C-9a), 72.4 (s, C-9), 117.2 (d, C-4), 118.6 (s, CN), 124.0 (s, Ar), 124.3, 124.9, 129.8 (3d, C-1, C-2, C-3), 141.7, 166.8 (2s, Ar, C-6)).

rac-(9*S,9a*R**,10*S**)-10-Allyl-9-(*tert*-butyl-dimethylsilyloxy)-9-methyl-6-oxo-7,8,9,9a,10-hexahydropyrido[1,2-a]indole-10-carbonitrile (19)**



Colourless solid: 93%, 143-146 °C (ν_{max}/cm^{-1}: 3080-3010 (ArH), 2950-2860 (CH), 2235 (CN), 1660 (CO), 1595 (C=C); δ_H (500 MHz, $CDCl_3$, Me_4Si): 0.19 (3H, s, $SiCH_3$), 0.26 (3H, s, $SiCH_3$), 0.96 (9H, s, $SiC(CH_3)_3$), 1.56 (3H, s, 9-CH_3), 2.01 (2H, m_c, 8-H), 2.57 (1H, m_c, 7-H), 2.73 (1H, ddd, J = 3.7, 8.6, 18.2 Hz, 7-H), 2.79 (1H, dd, J = 8.7, 13.9 Hz, 9-CH_2), 2.99 (1H, dd, J = 5.8, 13.9 Hz, 9-CH_2), 4.11 (1H, s, 9a-H), 5.20 (1H, d, J = 17.0 Hz, =CH_2), 5.24 (1H, d, J = 10.1 Hz, =CH_2), 5.63 (1H, dtd, J = 5.8, 8.8, 10.0 Hz, C*H*=CH_2), 7.14 (1H, t, J = 7.5 Hz, 2-H), 7.32 (1H, t, J = 7.8 Hz, 3-H), 7.39 (1H, d, J = 7.8 Hz, 1-H), 8.22 (1H, d, J = 8.1 Hz, 4-H); δ_C (100 MHz, $CDCl_3$, Me_4Si): -2.1, -1.6 (2q, $SiCH_3$), 18.1 (s, Si*C*$(CH_3)_3$), 20.3 (q, 9-CH_3), 25.9 (q, (C(*C*$H_3)_3$), 30.9, 38.4, 44.2 (3t, C-7, C-8, 10-CH_2), 46.3 (s, C-10), 71.5 (s, C-9), 73.9 (d, C-9a), 116.7 (d, C-4), 120.2 (s, CN), 121.7 (t, =CH_2), 123.9, 124.7 (2d, C-1, C-2), 128.3 (s, Ar), 130.1, 130.6 (2d, C-3, *C*H=CH_2), 141.6, 167.7 (2s, Ar, C-6); m/z (ESI-Tof): calcd for $C_{23}H_{32}N_2O_2Si$: 370.2197 $[M\text{-}CN]^+$, 419.2125 $[M+Na]^+$, found: 370.2213 $[M\text{-}CN]^+$, 419.2148 $[M+Na]^+$).

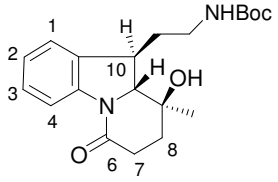
rac-(9*S,9a*R**,10*R**)-*tert*-Butyl-(9-hydroxy-9-methyl-6-oxo-7,8,9,9a,10-hexahydropyrido[1,2-a]indol-10-yl)methylcarbamate (20)**



Colourless solid: 91%; 204-206 °C (ν_{max}/cm^{-1}: 3310 (OH), 3045 (ArH), 2990-2855 (CH), 1705 (CO), 1625 (CO), 1590 (C=C); δ_H (400 MHz, $CDCl_3$, Me_4Si): 1.30 (3H, s, 9-CH_3), 1.44 (9H, s, C(C*H*$_3)_3$), 1.97 (1H, m_c, 8-H), 2.03 (1H, ddd, J = 2.6, 7.9, 12.9 Hz, 8-H), 2.58 (1H, ddd, J = 7.9, 10.9, 18.6 Hz, 7-H), 2.71 (1H, ddd, J = 2.6, 7.6, 18.6 Hz, 7-H), 3.45 (1H, dd, J = 8.8, 19.4 Hz, 10-CH_2), 3.57 (1H, m_c, 10-H), 3.90 (1H, m_c, 10-CH_2), 3.96 (1H, d, J = 9.8 Hz, 9a-H), 4.11 (1H, s, OH), 5.34 (1H, s, NH), 7.10 (1H, dt, J = 0.9, 7.4 Hz, 2-H), 7.22 (1H, d, J = 7.4 Hz, 1-H), 7.26 (1H, t, J ~ 7.7 Hz, 3-H), 8.21 (1H, d, J = 8.1 Hz, 4-H); δ_C (100 MHz, $CDCl_3$, Me_4Si): 20.0 (q, 9-CH_3), 28.3 (q, C(*C*$H_3)_3$), 31.3, 37.3 (2t, C-7, C-8), 43.2 (d, C-10), 69.8 (t, C*H*$_2$NHBoc), 70.1 (s, C-9), 80.1 (s, $CO_2C(CH_3)_3$), 116.9, 123.1, 124.3, 128.4 (4d, C-4,

C-1, C-2, C-3), 130.6, 142.6, 157.1, 167.8 (4s, 2Ar, *C*O^{t}Bu, C-6); m/z (ESI-Tof): calcd for $C_{19}H_{26}N_2O_4$: 369.1785 $[M+Na]^+$, found: 369.1790 $[M+Na]^+$).

rac-(9*S,9a*R**,10*R**)-*tert*-Butyl-2-(9-hydroxy-9-methyl-6-oxo-7,8,9,9a,10-hexahydropyrido[1,2-a]indol-10-yl)ethylcarbamate (21)**



Colourless solid: 97%; 136-138 °C (ν_{max}/cm^{-1}: 3330, 3245 (NH, OH), 3065-3005 (ArH), 2975-2880 (CH), 1685-1675, 1640 (CO), 1550 (C=C); δ_H (500 MHz, $CDCl_3$, Me_4Si): 1.21 (3H, s, 9-CH_3), 1.45 (9H, s, C(CH_3)$_3$)), 1.87 (1H, tdd, *J* = 4.7, 9.3, 14.0 Hz, 10-CH_2), 1.95 (1H, m_c, 8-H), 2.05 (2H, m_c, 8-H, 10-CH_2), 2.55 (2H, td, *J* = 8.1, 17.7 Hz, 7-H), 2.73 (1H, ddd, *J* = 5.0, 8.4, 17.7 Hz, 7-H), 3.19 (1H, m_c, C*H*$_2$NHBoc), 3.49 (1H, ddd, *J* = 2.9, 7.0, 16.0 Hz, 10-H), 3.64 (1H, m_c, C*H*$_2$NHBoc), 3.97 (1H, d, *J* = 7.0 Hz, 9a-H), 4.52 (1H, s, OH), 4.94 (1H, t, *J* = 6.0 Hz, NH), 7.06 (1H, dt, *J* = 1.0, 7.5 Hz, 2-H), 7.17 (1H, d, *J* = 7.5 Hz, 1-H), 7.21 (1H, t, *J* ~ 7.7 Hz, 3-H), 8.18 (1H, d, *J* = 8.0 Hz, 4-H); δ_C (125 MHz, $CDCl_3$, Me_4Si): 21.0 (q, 9-CH_3), 28.3 (q, C(*C*H$_3$)$_3$), 31.1, 36.3, 37.9, 38.4 (4t, C-7, C-8, 10-CH_2, *C*H$_2$NHBoc), 39.0 (d, C-10), 70.4 (s, C-9), 73.7 (d, C-9a), 80.1 (s, *C*(CH_3)$_3$), 116.4, 123.7, 124.0, 127.9 (4d, C-4, C-1, C-2, C-3), 133.5, 142.0, 157.1, 168.5 (4s, 2Ar, *C*O^{t}Bu, C-6); m/z (ESI-Tof): calcd. for $C_{20}H_{28}N_2O_4$: 383.1941 $[M+Na]^+$, 399.1680 $[M+K]^+$, found: 383.1924 $[M+Na]^+$, 399.1593 $[M+K]^+$).