

New Approaches for the Synthesis of Erythrinan Alkaloids

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Electronic supplementary information

Experimental

General Procedures

Melting points were determined in glass capillaries using a Stuart Scientific SMP3 melting point apparatus and are uncorrected. Infrared (IR) spectra were recorded using a Perkin Elmer 1600 series FTIR spectrometer with chloroform as solvent. Mass spectrometry, implementing electron impact (EI), chemical ionization (CI) and fast atom bombardment (FAB) with *meta*-nitrobenzyl alcohol as matrix, was performed using VG Micron Autospec or VG Micromass 70E spectrometers. Elemental analysis was performed using an Exeter Analytical CE-440. Optical rotations were recorded using a Jasco DIP-370 digital polarimeter with a 5 cm path length. Concentrations for optical rotation measurements are given in g/100 cm³. ¹H NMR and ¹³C NMR experiments were recorded using Bruker AV400 or Bruker DRX500 NMR spectrometers. Chemical shifts are quoted in ppm and coupling constants (*J*) are quoted in Hz. The following abbreviations apply; (br) broad, (s) singlet, (d) doublet, (t) triplet, (q) quartet, (m) multiplet, (dd) double doublet, etc. The chemical shifts of multiplets corresponding to a single proton are quoted as a point, representing the centre of the multiplet. Where the signals for two or more non-equivalent protons overlap, a range is quoted. Column chromatography was performed using Merck silica gel 60 (230-400 mesh). Thin layer chromatography (TLC) was conducted using precoated plastic backed silica gel plates (Polygram SIL G/UV254) with 0.2 mm thickness, with observation by KMnO₄, and under UV (254 nm). Enantiomeric excesses were determined by chiral HPLC with a Hewlett-Packard LC1100 using DAICEL chiralcel-OD and OD-H columns and using HPLC grade 2-propanol and hexane as eluents. THF and diethyl ether were freshly distilled from sodium-benzophenone; dichloromethane and trim

ethylsilylchloride were distilled from calcium hydride. All other solvents and reagents were used as received from commercial suppliers unless stated otherwise. A mixture of ethanol and liquid N₂ was used to obtain -105 °C (bath temperature) whereas acetone and solid CO₂ was used to obtain -78 °C (bath temperature). Where necessary, reactions requiring anhydrous conditions were performed in dry solvents in flame-dried or oven-dried apparatus under a dry nitrogen atmosphere.

The preparation and spectral data of compounds **6**, **7**, (+)-**8**, (-)-**11**, (-)-**12**, (-)-**13**, (+)-**14**, (+)-**15**, can be found in our previous paper (*Synthesis*, **2005**, *19*, 3287)

6,7-Dichloro-3-oxa-bicyclo[3.2.0]heptane-2,4-dione 26

A solution of maleic anhydride **25** (5.1 g, 52.8 mmol) in anhydrous EtOAc (260 mL) was degassed with N₂ before *trans*-1, 2-dichloroethylene (4.0 mL, 58.0 mmol) was added. The reaction mixture was then irradiated in a pyrex photoreactor using light from a 400 W medium Hg lamp, with regular monitoring by ¹H NMR spectroscopy. After the reaction was completed the solvent was evaporated and Et₂O was added, and a solid was precipitated. Filtration gave **26** as a powder (3.1 g, 30 %). ¹H NMR spectroscopy indicated that **26** was a mixture of isomers which was used for the next step without further purification.

(1*S*,5*R*)-3-(3,4-Dimethoxyphenethyl)-6,7-dichloro-3-aza-bicyclo[3.2.0]heptane- 2,4-dione 28

To the solution of anhydride **26** (390 mg, 2 mmol) in acetic acid (6 mL) was added slowly 2-(3,4-dimethoxyphenyl)ethylamine **27** (398.7 mg, 2.2 mmol). The resulting reaction mixture was then refluxed overnight. The mixture was cooled to room temperature and water was added until a precipitate was formed. Filtered and the resulting solid was dissolved in EtOAc (100 mL) and

washed with saturated brine (10 mL). The organic phase was dried over anhydrous Na_2SO_4 and concentrated *in vacuo* to give a colourless solid **28** as a mixture of isomers (680 mg, 95%): ν_{max} (CHCl_3)/ cm^{-1} 2938, 2838, 1778, 1716, 1391, 1357, 1149, 906; δ_{H} (400 MHz, CDCl_3) 2.97 (t, J 7.4, 2 H, PhCH_2), 3.47 (d, J 2.6, 2 H, CHCH), 3.83 (t, J 7.4, 2 H, NCH_2), 3.87 (s, 3 H, OCH_3), 3.88 (s, 3 H, OCH_3), 4.15 (d, J 2.6, 2 H, CHClCHCl), 6.68-6.78 (m, 3 H, ArH); δ_{C} (100.6 MHz, CDCl_3): 32.2 (ArCH_2), 39.4 (NCH_2), 47.5 (CH), 56.0 (OCH_3), 56.1 (OCH_3), 56.4 (CH), 111.1 (ArCH), 112.2 (ArCH), 121.1 (ArCH), 129.4 (ArC), 148.2 (ArC), 149.1 (ArC), 173.9 (NC=O); HRMS (ESI) found $[\text{M}]^+$, 357.0535. $\text{C}_{16}\text{H}_{17}\text{NO}_4\text{Cl}_2$ requires M, 357.0536.

(1*S*,5*R*)-3-(3,4-Dimethoxyphenethyl)-3-aza-bicyclo[3.2.0]hept-6-ene-2,4-dione 24

Zinc powder (1.5 g, 23 mmol) was activated by washing with 2 M HCl solution (10 mL), water (10 mL), ethanol (10 mL) and ether (10 mL), and then dried under reduced pressure using toluene (10 mL) to remove the water. The activated zinc powder was added in one portion to the solution of dichloride **28** (250 mg, 0.92 mmol) and acetic anhydride (1.1 g, 11 mmol) in toluene (15 mL). The resulting reaction mixture was then stirred at 85 °C for one day. The reaction mixture was then cooled to room temperature and filtered. The filtrate was concentrated *in vacuo* and purified by flash column chromatography (eluent: petroleum ether/AcOEt = 1/1) to give the desired product **24** as a colourless powder (160 mg, 80%): mp 101-102 °C; ν_{\max} . (CHCl₃)/cm⁻¹ 2938, 1703, 1392, 1154, 908; δ_{H} (400 MHz, CDCl₃) 2.80 (t, *J* 7.6, 2 H, PhCH₂), 3.68 (t, *J* 7.6, 2 H, NCH₂), 3.74 (s, 2 H, CHCH), 3.83 (s, 3 H, OCH₃), 3.86 (s, 3 H, OCH₃), 6.37 (s, 2 H, CH=CH), 6.71-6.77 (m, 3 H, ArH); δ_{C} (100.6 MHz, CDCl₃) 32.9 (ArCH₂), 39.6 (NCH₂), 47.5 (CH), 55.9 (OCH₃), 111.2 (ArCH), 112.1 (ArCH), 121.0 (ArCH), 130.2 (ArC), 139.4 (CH=), 147.7 (ArC), 148.8 (ArC), 174.5 (NC=O); ESIMS *m/z* (%) 310.1 ([M+Na]⁺, 100), 288.1 ([M+H]⁺, 28); HRMS (ESI) found M⁺, 287.1160. C₁₆H₁₇NO₄ requires *M*, 287.1158.

(1*S*,5*R*)-3-(3,4-Dimethoxyphenethyl)-1-(trimethylsilyl)-3-aza-bicyclo[3.2.0]hept-6-ene-2,4-dione 29

The *bis*-lithium chiral base **10** solution was prepared by addition of *n*-BuLi (1.6 M in THF, 0.66 mL, 1.05 mmol) to the solution of corresponding chiral amine (253 mg, 0.6 mmol) in THF (4 mL). After cooling to -100 °C, the chiral base was added dropwise by cannula to the solution of imide **24**

(143 mg, 0.5 mmol) and TMSCl (0.64 mL, 5 mmol) in THF (8 mL). The resulting reaction mixture was stirred at the same temperature for 4 hours. Saturated aqueous NaHCO₃ (5 mL) solution was added and diluted with EtOAc (100 mL). The organic phase was washed with water (10 mL), brine (10 mL), dried over MgSO₄ and concentrated *in vacuo*. The crude product was purified by silica column chromatography (eluent: petroleum ether/AcOEt = 2/1 to 1/1) to give the product **29** (88 mg, 88%) as a yellow oil: $[\alpha]_D^{25} +131$ (*c* 4.50, CHCl₃); ν_{\max} . (CHCl₃)/cm⁻¹ 2938, 2838, 1755, 1682, 1593, 1387, 1357, 986; δ_H (500 MHz, CDCl₃) 0.09 (s, 9 H, Si(CH₃)₃), 2.77 (t, *J* 7.5, 2 H, PhCH₂), 3.47 (d, *J* 1.0, 1 H, NCOCH), 3.59-3.69 (m, 2 H, NCH₂), 3.69 (s, 3 H, OCH₃), 3.83 (s, 3 H, OCH₃), 6.31 (dd, *J* 2.5, 1.0, 1 H, CH=CH), 6.39 (d, *J* 2.5, 1 H, CH=CH), 6.69-6.74 (m, 3 H, ArH); δ_C (125 MHz, CDCl₃) -3.5 (SiCH₃), 33.0 (ArCH₂), 39.7 (NCH₂), 50.0 (CH), 52.4 (CSi), 55.9 (OCH₃), 55.9 (OCH₃), 111.2 (ArCH), 112.1 (ArCH), 121.0 (ArCH), 130.3 (ArC), 136.0 (CH=), 142.6 (CH=), 147.7 (ArC), 148.8 (ArC), 174.3 (NC=O), 176.6 (NC=O); HRMS (ESI) found $[M+H]^+$, 360.1626. C₁₉H₂₅NO₄Si requires $[M+H]$, 360.1590; The ee was determined as > 99% by HPLC (chiral OD column, 4% *i*PrOH in hexane, 0.6 ml/min), the retention times were 29.5 min (major), and 32.4 min (minor). The absolute stereochemistry of this product was assigned by analogy with known examples.

**(1*R*,5*S*)-3-(3,4-Dimethoxyphenethyl)-4-(3-butenyl)-4-hydroxy-3-aza-bicyclo-
[3.2.0]hept-6-en-2-one 23**

Grignard reagent was prepared as follows: Magnesium turnings (612 mg, 26 mmol) were placed in a three-necked round bottle, and THF (25 mL) was added. The solution of 4-bromo-1-butene (2 mL, 20 mmol) in THF (15 mL) was then added dropwise to the above suspension. After the

addition the reaction mixture was kept at gentle reflux for another 1 hour. After cooling to room temperature the Grignard reagent was added dropwise to the imide **24** (1.5 g, 5.1 mmol) at $-78\text{ }^{\circ}\text{C}$. The resulting solution was then warmed to rt slowly until the reaction was completed. The reaction was quenched with saturated aqueous NaHCO_3 solution (10 mL) before dilution with EtOAc (150 mL). The organic phase was washed with water (10 mL) and brine (10 mL). After being dried and concentrated, the residue was purified by flash silica column chromatography (eluent: petroleum ether/AcOEt = 1:1) to give the hydroxy lactam **23** (1.5 g, 83%) as a colourless oil: ν_{max} (CHCl_3)/ cm^{-1} 3584, 2937, 1673, 1492, 1028; δ_{H} (400 MHz, *d*-acetone) 1.48-1.56 (m, 1 H, $\text{CH}_A\text{H}_B\text{COH}$), 1.92-2.04 (m, 1 H, $\text{CH}_A\text{H}_B\text{COH}$), 2.20-2.48 (m, 2 H, $\text{CH}_2\text{C}=\text{}$), 2.80-3.00 (m, 2 H, ArCH₂), 3.31-3.52 (m, 4 H, NCH₂, CHCH), 3.83 (s, 3 H, OCH₃), 3.86 (s, 3 H, OCH₃), 4.94-5.07 (m, 3 H, OH, $\text{CH}_2=\text{}$), 5.85-6.02 (m, 1 H, $\text{CH}=\text{CH}_2$), 6.74 (d, *J* 2.0, 1 H, $\text{CH}=\text{CH}$), 6.76 (d, *J* 2.0, 1 H, $\text{CH}=\text{CH}$), 6.80-6.87 (m, 3 H, ArH); δ_{C} (100 MHz, *d*-acetone) 30.0 (CH_2), 35.9 (CH_2), 35.9 (CH_2), 42.0 (CH_2), 49.2 (CH), 51.4 (CH), 56.1 (OCH₃), 56.2 (OCH₃), 89.8 (COH), 113.0 (ArCH), 113.8 (ArCH), 114.8 ($\text{CH}_2=\text{}$), 121.6 (ArCH), 133.3 (ArC), 139.3 ($\text{CH}=\text{}$), 140.6 ($\text{CH}=\text{}$), 142.1 ($\text{CH}=\text{}$), 149.0 (ArC), 150.0 (ArC), 174.3 (NC=O); ESIMS *m/z* (%) 366.2 ($[\text{M}+\text{Na}]^+$, 100), 326.2 ($[\text{M}-\text{H}_2\text{O}]^+$, 97); HRMS (ESI) found M^+ , 343.1784. $\text{C}_{20}\text{H}_{25}\text{NO}_4$ requires *M*, 343.1784.

(2*S*,3*S*,14*R*)-6,7-Dimethoxy-3-(3-butenyl)-12-azatetracyclo[11.2.0^{2,14}.0^{3,12}.0^{4,9}]-

4,6,8,15-tetraen-13-one **22**

TMSOTf (6 mL, 33 mmol) was added in one portion to the solution of hydroxyl lactam **23** (5.7 g, 16.5 mmol) in CH_2Cl_2 (50 mL) at $-78\text{ }^{\circ}\text{C}$. The resulting reaction mixture was left in a cold room ($-4\text{ }^{\circ}\text{C}$) overnight. Water (5 mL) was added and the mixture was extracted with EtOAc (200 mL).

The organic phase was washed with saturated aq. NaHCO₃ (10 mL) and water (10 mL), dried over anhydrous Na₂SO₄ and concentrated *in vacuo*. The crude product was purified by flash silica column chromatography (eluent: petroleum ether/AcOEt = 2:1) to give a colourless oil **22** (5.1 g, 95%) as a mixture of diastereomers in a ratio of 20:1: ν_{\max} . (CHCl₃)/cm⁻¹ 2938, 2856, 1667, 1360, 1124, 904; δ_{H} (400 MHz, CDCl₃) 1.90-1.92 (m, 1 H, CCH_AH_B), 2.04-2.07 (m, 1 H, CCH_AH_B), 2.15-2.18 (m, 2 H, CH₂CH=), 2.64 (ddd, *J* 16.4, 5.0, 1.2, 1 H, ArCH_ACH_B), 3.05-3.10 (ddd, *J* 16.4, 12.0, 7.2, 1 H, ArCH_ACH_B), 3.11-3.21 (ddd, *J* 14.0, 12.0, 5.0, 1 H, NCH_ACH_B), 3.51 (d, *J* 4.0, 1 H, CHCH), 3.72 (d, *J* 4.0, 1 H, CHCH), 3.83 (s, 3 H, OCH₃), 3.88 (s, 3 H, OCH₃), 4.30 (ddd, *J* 14.0, 7.2, 1.2, 1 H, NCH_ACH_B), 4.98 (m, 2 H, CH₂=), 5.75-5.78 (m, 1 H, CH=CH₂), 6.41 (d, *J* 2.4, 1 H, CH=CH), 6.50 (dd, *J* 2.4, 0.8, 1 H, CH=CH), 6.56 (s, 1 H, ArH), 6.65 (s, 1 H, ArH); δ_{C} (100 MHz, CDCl₃) 26.8 (CH₂), 29.6 (CH₂), 34.9 (CH₂), 37.9 (CH₂), 48.8 (CH), 50.1 (CH), 55.9 (OCH₃), 56.2 (OCH₃), 62.1 (C), 108.7 (ArCH), 112.2 (ArCH), 115.0 (CH₂=), 126.5 (ArC), 132.1 (ArC), 137.4 (CH=), 139.0 (CH=), 141.0 (CH=), 146.8 (ArC), 148.1 (ArC), 173.1 (NC=O); ESIMS *m/z* (%) 326.1 ([M+H]⁺, 100); HRMS (ESI) found M⁺, 325.1668. C₂₀H₂₃NO₃ requires *M*, 325.1678.

(4a*S*,5*R*,13b*S*)-11,12-Dimethoxy-5-vinyl-1,2,4a,5,8,9-hexahydroindolo[1-*a*]-isoquinolin-6-one

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Cyclobutene imide **22** (233 mg, 0.72 mmol) was dissolved in dry CH₂Cl₂ (50 mL) so that the concentration reached approximately 0.01 M. This solution was degassed under argon. Ethylene was then bubbled through the solution for 5 min. Grubbs first generation catalyst **18** (59 mg, 0.07 mmol) was then added. Ethylene was again passed through the solution for 5 min, and the solution was then stirred under an ethylene atmosphere (fitted balloon) at 35 °C until TLC revealed

completion of the reaction. The mixture was cooled to room temperature and ethyl vinyl ether (2 mL) was added. The reaction mixture was stirred for another 1 hour then concentrated. The crude product was purified by silica column chromatography (eluent: petroleum ether/AcOEt = 3/1 to 1/1) to give the major product **21** (144 mg, 62%): $\nu_{\text{max.}}$ (CHCl_3)/ cm^{-1} 2996, 2846, 1662, 1463, 1362, 1106, 908; δ_{H} (400 MHz, CDCl_3) 1.74-1.81 (m, 1 H), 2.00-2.06 (m, 2 H), 2.16-2.22 (m, 1 H), 2.72-2.78 (ddd, 1 H, J 16.4, 6.0, 3.2, ArCH_AH_B), 2.94-3.02 (m, 1 H, ArCH_AH_B), 3.10 (d, J 8.0, 1 H, $\text{CHCH}=\text{CH}$), 3.29-3.36 (m, 2 H, CHCO , NCH_AH_B), 3.82 (s, 3 H, OCH_3), 3.86 (s, 3 H, OCH_3), 4.10-4.21 (ddd, J 13.2, 7.2, 3.2, 1 H, NCH_AH_B), 5.26-5.32 (m, 2 H, $\text{CH}=\text{CH}_2$), 5.73-5.86 (m, 2 H, $\text{CH}=\text{CH}_2$, $\text{CH}=\text{CHCH}$), 6.05-6.12 (m, 1 H, $\text{CH}=\text{CHCH}$), 6.61 (s, 1 H, ArH), 6.73 (s, 1 H, ArH); δ_{C} (100 MHz, CDCl_3) 22.2 (CH_2), 27.1 (CH_2), 33.3 (CH_2), 35.1 (CH_2), 43.3 (CH), 50.8 (CH), 55.9 (OCH_3), 56.0 (OCH_3), 61.0 (C), 108.1 (ArCH), 111.8 (ArCH), 119.3 ($\text{CH}_2=$), 125.2 (ArC), 126.5 ($\text{CH}=\text{}$), 128.8 ($\text{CH}=\text{}$), 133.5 (ArC), 133.8 ($\text{CH}=\text{}$), 147.6 (ArC), 148.0 (ArC), 172.8 ($\text{NC}=\text{O}$); ESIMS m/z (%) 326.2 ($[\text{M}+\text{H}]^+$, 100); HRMS (ESI) found M^+ , 325.1670. $\text{C}_{20}\text{H}_{23}\text{NO}_3$ requires M , 325.1678.

(3R,4S,4aS,5R,13bS)-3,4-Dihydroxy-11,12-dimethoxy-5-vinyl-1,2,3,4,4a,5,8,9-octahydroindolo[1-a]isoquinolin-6-one 33

AD-mix- α (160 mg) was added into the solution of terminal olefin **21** (20 mg, 0.06 mmol) in *t*-BuOH (1.5 mL) and water (1.5 mL) at room temperature. The resulting solution was then stirred at rt overnight before water (5 mL) was added. The mixture was extracted with CH_2Cl_2 (30 mL). The organic phase was washed with brine (5 mL), dried over MgSO_4 and concentrated *in vacuo*. The crude product was purified by flash silica column chromatography (eluent: EtOAc) to give the product **33** (17.1 mg, 77%): $\nu_{\text{max.}}$ (CHCl_3)/ cm^{-1} 3582, 2960, 2927, 1723, 1688, 1463, 1382, 1264,

1101, 1050, 874; δ_{H} (400 MHz, CDCl_3) 1.55-1.65 (m, 1 H, $\text{CCH}_2\text{CH}_A\text{H}_B$), 1.82-1.93 (m, 2 H, $\text{CCH}_A\text{H}_B\text{CH}_A\text{H}_B$), 2.16-2.23 (m, 1H, $\text{CCH}_A\text{H}_B\text{CH}_2$), 2.52 (dd, J 16.5, 5.1, 1 H, ArCH_ACH_B), 2.85 (t, J 7.6, 1 H, CHCHOH), 3.07-3.18 (m, 2 H, ArCH_ACH_B , CHCH=), 3.19-3.28 (m, 1 H, NCH_ACH_B), 3.78 (dd, J 8.3, 3.1, 1 H, CHCHOH), 3.84 (s, 3 H, OCH_3), 3.89 (s, 3 H, OCH_3), 4.05 (t, J 2.3, 1 H, CHOHCH_2), 4.18-4.23 (m, 1 H, NCH_AH_B), 5.41 (dd, 1 H, J 19.0, 1.2, 1 H, $\text{CH}_A\text{H}_B=$), 5.46 (dd, J 10.4, 1.2, 1 H, $\text{CH}_A\text{H}_B=$), 6.00 (ddd, J 19.0, 10.4, 8.6, 1 H, $\text{CH}=\text{CH}_2$), 6.51 (s, 1 H, ArH), 6.86 (s, 1 H, ArH); δ_{C} (100 MHz, CDCl_3) 25.2 (CH_2), 25.7 (CH_2), 29.2 (CH_2), 35.8 (CH_2), 47.1 (CH), 49.1 (CH), 55.9 (OCH_3), 56.2 (OCH_3), 63.5 (C), 68.1 (CHOH), 70.3 (CHOH), 108.1 (ArCH), 112.0 (ArCH), 122.4 ($\text{CH}_2=$), 126.1 (ArC), 132.4 ($\text{CH}=\text{}$), 132.5 (ArC), 147.6 (ArC), 148.2 (ArC), 177.9 ($\text{NC}=\text{O}$); ESIMS m/z (%) 360.2 ($[\text{M}+\text{H}]^+$, 66), 382.2 ($[\text{M}+\text{Na}]^+$, 66); HRMS (ESI) found M^+ , 359.1733. $\text{C}_{20}\text{H}_{25}\text{NO}_5$ requires M , 359.1725.

**(4a*R*,13b*S*)-5-Hydroxy-11,12-dimethoxy-5-vinyl-1,2,4a,5,8,9-hexahydroindolo-
[1-*a*]isoquinolin-6-one **34****

To a stirred solution of imide **21** (85 mg, 0.26 mmol) in 1, 4-dioxane (6 mL) was added SeO_2 (31.9 mg, 0.29 mmol). The resulting reaction mixture was stirred at reflux for 2 hours and then cooled to room temperature. The mixture was concentrated *in vacuo* and purified by flash chromatography (eluent: petroleum ether/EtOAc = 1/3) to give the allylic alcohol **34** (55 mg, 62%) and dehydration product **35** (11 mg, 13%). Major product **34**: oil; more polar; ν_{max} (CHCl_3)/ cm^{-1} 3552, 2936, 2836, 1683, 1454, 1363, 908; δ_{H} (500 MHz, CDCl_3) 2.02-2.26 (m, 4 H, CCH_2CH_2), 2.87-3.01 (m, 3 H, CH, Ar CH_2), 3.42-3.48 (m, 1 H, NCH_AH_B), 3.77 (s, 3 H, OCH_3), 3.85 (s, 3 H, OCH_3), 4.15-4.22 (m, 1 H, NCH_AH_B), 5.39 (dd, J 10.5, 1.0, 1 H, $\text{CH}=\text{CH}_A\text{H}_B$), 5.50 (dd, J 17.5, 1.0,

1 H, CH=CH_AH_B), 5.98 (dd, *J* 17.5, 10.5, 1 H, CH=CH₂), 6.09-6.12 (m, 1 H, CH₂CH=CH), 6.20 (dd, *J* 10.5, 6.5, 1 H, CH₂CH=CH), 6.71 (s, 1 H, ArH), 6.79 (s, 1 H, ArH); δ_C (125 MHz, CDCl₃) 22.8 (CH₂), 27.0 (CH₂), 31.8 (CH₂), 35.8 (CH₂), 51.4 (CH), 55.9 (OCH₃), 56.0 (OCH₃), 58.6 (C), 80.0 (C), 107.9 (ArCH), 111.5 (ArCH), 116.4 (CH₂=), 124.4 (C), 125.6 (CH=), 129.3 (CH=), 133.4 (C), 137.6 (CH=), 147.7 (C), 148.0 (C), 171.9 (NC=O); ESIMS *m/z* (%) 364.2 ([M+Na]⁺, 100); HRMS (ESI) found M⁺, 341.1626. C₂₀H₂₃NO₄ requires *M*, 341.1627.

Dehydration product **35**: oil; less polar; ν_{\max} . (CHCl₃)/cm⁻¹ 2936, 1669, 1464, 1362, 1109, 1043; δ_H (500 MHz, CDCl₃) 1.83 (td, *J* 9.6, 4.4, 1 H, CCH₂CH_AH_B), 2.21-2.19 (m, 1 H, CCH₂CH_AH_B), 2.32-2.36 (m, 1 H, CCH_AH_BCH₂), 2.41-2.47 (m, 1 H, CCH_AH_BCH₂), 2.99 (td, *J* 11.2, 2.0, 2 H, ArCH₂), 3.56 (dt, *J* 10.4, 5.6, 1 H, NCH_AH_B), 3.78 (s, 3 H, OCH₃), 3.86 (s, 3 H, OCH₃), 4.11 (td, *J* 10.4, 5.6, 1 H, NCH_AH_B), 5.46 (dd, *J* 9.0, 2.0, 1 H, CH=CH_AH_B), 6.30-6.34 (m, 1 H, CH=CH), 6.46 (dd, *J* 14.0, 2.0, 1 H, CH=CH_AH_B), 6.59 (dd, *J* 14.0, 9.0, 1 H, CH=CH₂), 6.69 (s, 1 H, ArH), 7.02 (s, 1 H, ArH), 7.01-7.06 (m, 1 H, CH=CH); δ_C (125 MHz, CDCl₃) 24.7 (CH₂), 27.2 (CH₂), 35.0 (CH₂), 36.9 (CH₂), 55.9 (OCH₃), 56.0 (OCH₃), 62.3 (C), 108.8 (ArCH), 112.0 (ArCH), 120.5 (CH₂=), 122.6 (CH=), 125.2 (C), 125.6 (CH=), 126.3 (C), 128.9 (C), 135.6 (CH=), 146.8 (C), 148.2 (C), 150.1 (C), 170.2 (NC=O); ESIMS *m/z* (%) 324.2 ([M+H]⁺, 54), 346.1 ([M+Na]⁺, 100); HRMS (ESI) found M⁺, 323.1521. C₂₀H₂₁NO₃ requires *M*, 323.1521.

(4a*S*,5*R*,13b*S*)-11,12-Dimethoxy-5-(2-methylprop-1-enyl)-1,2,4a,5,8,9-

hexahydroindolo[1-*a*]isoquinolin-6-one **37**

Imide **21** (40 mg, 0.12 mmol) was dissolved in CH₂Cl₂ (2 mL) before 2-methyl-2-butene (6 mL)

was added. The Hoveyda-Grubbs catalyst (15 mg, 0.025 mmol) was then added. The resulting reaction mixture was refluxed under nitrogen atmosphere until the reaction was completed. The reaction mixture was concentrated *in vacuo* and purified by silica column chromatography (eluent: petroleum ether/EtOAc = 3/1) to give the partially separated mixtures of two products **37** (30 mg, 70%) and **38** (7 mg, 15%). Major product **37**: colourless oil; less polar; ν_{\max} . (CHCl₃)/cm⁻¹ 2935, 2854, 1668, 1463, 1362, 1115, 872; δ_{H} (400 MHz, CDCl₃) 1.71 (s, 3 H, CH₃), 1.77 (s, 3 H, CH₃), 1.75-2.24 (m, 4 H, CH₂CH₂), 2.68-2.77 (m, 1 H, ArCH_AH_B), 2.95-3.14 (m, 2 H, CHCH=CH, ArCH_AH_B), 3.26-3.34 (m, 1 H, NCH_AH_B), 3.51 (t, *J* 9.6, 1 H, CHCH=C), 3.83 (s, 3 H, OCH₃), 3.86 (s, 3 H, OCH₃), 4.17-4.24 (m, 1 H, NCH_AH_B), 5.15 (d, *J* 9.6, 1 H, CH=C), 5.70-5.76 (m, 1 H, CH=CH), 5.99-6.07 (m, 1 H, CH=CH), 6.61 (s, 1 H, ArH), 6.73 (s, 1 H, ArH); δ_{C} (100 MHz, CDCl₃) 18.6 (CH₃), 22.1 (CH₂), 26.0 (CH₃), 27.1 (CH₂), 33.7 (CH₂), 35.1 (CH₂), 43.4 (CH), 45.6 (CH), 55.9 (OCH₃), 56.1 (OCH₃), 61.1 (C), 108.2 (ArCH), 111.9 (ArCH), 119.8 (CH=), 125.4 (C), 126.9 (CH=), 128.2 (CH=), 133.8 (C), 136.8 (C), 147.6 (C), 148.0 (C), 174.8 (NC=O); ESIMS *m/z* (%) 354.2 ([M+H]⁺, 100), 376.2 ([M+Na]⁺, 42); HRMS (ESI) found M⁺, 353.1991. C₂₂H₂₇NO₃ requires *M*, 353.1998. Minor product **38**: colourless oil; more polar; ν_{\max} . (CHCl₃)/cm⁻¹ 2935, 2854, 1674, 1463, 1362, 1120, 1044, 906, 868; δ_{H} (400 MHz, CDCl₃) 1.63 (s, 3 H, CH₃), 1.71 (s, 3 H, CH₃), 1.88-2.29 (m, 5 H, CH_AH_BCH=C, CCH₂CH₂), 2.41-2.70 (m, 3 H, ArCH_AH_B, CHCO, CH_AH_BCH=C), 2.97-3.14 (m, 2 H, CHCH=CH, ArCH_AH_B), 3.20-3.30 (m, 1 H, NCH_AH_B), 3.83 (s, 3 H, OCH₃), 3.86 (s, 3 H, OCH₃), 4.20-4.25 (m, 1 H, NCH_AH_B), 5.20 (t, *J* 6.1, 1 H, CH=C), 5.80-5.81 (m, 1 H, CH=CH), 6.01-6.02 (m, 1 H, CH=CH), 6.58 (s, 1 H, ArH), 6.70 (s, 1 H, ArH); δ_{C} (100 MHz, CDCl₃) 18.2 (CH₃), 21.8 (CH₂), 25.9 (CH₃), 26.8 (CH₂), 26.9 (CH₂), 33.7 (CH₂), 35.1 (CH₂), 42.1 (CH), 46.3 (CH), 55.9 (OCH₃), 56.2 (OCH₃), 61.3 (C), 108.2 (ArCH), 112.0 (ArCH),

122.5 (CH=), 125.7 (C), 126.0 (CH=), 128.7 (CH=), 132.8 (C), 133.7 (C), 147.6 (C), 148.0 (C), 176.3 (NC=O); ESIMS m/z (%) 368.2 ($[M+H]^+$, 81), 390.2 ($[M+Na]^+$, 100); HRMS (ESI) found M^+ , 367.2162. $C_{23}H_{29}NO_3$ requires M , 367.2147.

(4a*S*,5*R*,13b*S*,*E*)-11,12-Dimethoxy-5-styryl-1,2,4a,5,8,9-hexahydroindolo[1-*a*]-isoquinolin-6-one 40

The Grubbs second generation catalyst **39** (12.6 mg, 10 mol %) was added to the solution of imide **21** (50 mg, 0.15 mmol) and styrene (0.27 ml, 2.3 mmol) in CH_2Cl_2 (10 mL). The resulting reaction mixture was then stirred at reflux under nitrogen atmosphere overnight. The reaction mixture was cooled and concentrated *in vacuo*. The crude product was purified by silica column chromatography (eluent: petroleum ether/EtOAc = 2/1) to give the product **40** (31 mg, 51%, 72% based on recovered starting material) as a colourless oil: ν_{max} . ($CHCl_3$)/ cm^{-1} 2936, 2846, 1672, 1362, 1106; δ_H (500 MHz, $CDCl_3$) 1.82-1.89 (m, 1 H, $CCH_2CH_AH_B$), 2.03-2.12 (m, 2 H, $CCH_AH_BCH_AH_B$), 2.19-2.27 (m, 1 H, $CCH_AH_BCH_2$), 2.75-2.82 (m, 1 H, $ArCH_AH_B$), 2.98-3.08 (m, 1 H, $ArCH_AH_B$), 3.15-3.20 (m, 1 H, NCH_AH_B), 3.30-3.40 (m, 1 H, $CHCHCO$), 3.49 (t, J 9.0, 1 H, $CHCHCO$), 3.83 (s, 3 H, OCH_3), 3.86 (s, 3 H, OCH_3), 4.20-4.26 (m, 1 H, NCH_AH_B), 5.90 (dt, J 10.2, 2.0, 1 H, $CH_2CH=CH$), 6.07-6.12 (m, 1 H, $CH_2CH=CH$), 6.18 (dd, J 15.7, 9.0, 1 H, $CH=CHPh$), 6.62 (d, J 15.7, 1 H, $CH=CHPh$), 6.63 (s, 1 H, ArH), 6.75 (s, 1 H, ArH), 7.20-7.40 (m, 5 H, ArH); δ_C (125 MHz, $CDCl_3$) 22.2 (CH_2), 27.1 (CH_2), 33.5 (CH_2), 35.2 (CH_2), 43.8 (CH), 49.9 (CH), 55.9 (OCH_3), 56.0 (OCH_3), 61.1 (C), 108.1 (CH), 111.8 (CH), 125.2 (C), 125.4 (CH), 126.5 (2 x CH), 127.5 (CH), 128.3 (CH), 128.5 (CH), 128.9 (CH), 129.0 (CH), 133.5 (C), 134.0 (CH), 137.0 (C), 147.6 (C), 148.0 (C), 173.0 (NC=O); ESIMS m/z (%) 402.2 ($[M+H]^+$, 100), 424.2 ($[M+Na]^+$, 61); HRMS (ESI) found M^+ ,

401.1991. C₂₆H₂₇NO₃ requires *M*, 401.2006.

2-((4a*S*,5*R*,13b*S*)-11,12-Dimethoxy-6-oxo-1,2,4a,5,8,9-hexahydroindolo-[1-*a*]isoquinolin-5-yl)acetaldehyde **41**

The suspension of PdCl₂ (17.4 mg, 0.1 mmol) and CuCl (40.3 mg, 0.4 mol) in DMF (2.0 mL) and water (0.4 mL) was degassed with oxygen. The mixture was then stirred at room temperature for 4 hours. Imide **21** (145 mg, 0.45 mmol) in DMF (0.8 mL) was added and the resulting reaction mixture was stirred under oxygen atmosphere for 20 h. The reaction mixture was diluted with EtOAc (100 mL). The organic phase was washed with water (3 x 10 mL), brine (10 mL), dried over MgSO₄ and concentrated *in vacuo*. The crude product was purified by silica column chromatography (eluent: petroleum ether/AcOEt = 1/1) to give the product as a colourless oil **41** (119 mg, 78%): ν_{\max} (CHCl₃)/cm⁻¹ 2935, 2835, 1723, 1694, 1456, 1392, 1361, 1120, 870; δ_{H} (500 MHz, CDCl₃) 1.73-1.78 (m, 1 H), 1.94-2.13 (m, 3 H), 2.64-2.71 (m, 2 H), 2.83-3.02 (m, 2 H), 3.12-3.28 (m, 3 H), 3.79 (s, 3 H, OCH₃), 3.81 (s, 3 H, OCH₃), 4.10-4.19 (m, 1 H, NCH_AH_B), 5.57-5.60 (m, 1 H, CH=), 6.01-6.04 (m, 1 H, CH=), 6.56 (s, 1 H, ArH), 6.66 (s, 1 H, ArH), 9.82 (s, 1 H, CHO); δ_{C} (125 MHz, CDCl₃) 21.7 (CH₂), 26.8 (CH₂), 33.8 (CH₂), 35.0 (CH₂), 39.9 (CH), 41.4 (CH), 42.6 (CH₂), 55.8 (OCH₃), 56.0 (OCH₃), 61.5 (C), 108.0 (CH), 111.8 (CH), 125.1 (C), 125.4 (CH), 130.0 (CH), 133.0 (C), 147.6 (C), 148.0 (C), 174.7 (NC=O), 200.4 (CHO); HRMS (ESI) found M^+ , 341.1627. C₂₀H₂₃NO₄ requires *M*, 341.1626.

(4a*S*,5*S*,13b*S*,*E*)-5-(2-(*tert*-Butyldimethylsilyloxy)vinyl)-11,12-dimethoxy-

1,2,4a,5,8,9-hexahydroindolo[1-*a*]isoquinolin-6-one **42**

TBSOTf (0.32 mL, 1.4 mmol) was added dropwise to the solution of aldehyde **41** (240 mg, 0.7 mmol) in CH₂Cl₂-Et₃N (4 mL/0.2 mL) at -78 °C under nitrogen atmosphere and the resulting reaction mixture was then stirred at this temperature for 5 hours. The reaction mixture was diluted with CH₂Cl₂ (50 mL). The organic phase was washed with water (10 mL), brine (10 mL), then dried over MgSO₄ and concentrated *in vacuo*. The crude product was purified by silica column chromatography (eluent: petroleum ether/AcOEt: 2/1) to give the product as a pale yellow foam **42** (100 mg, 31%), 42 mg starting material aldehyde **41** was recovered. colourless oil; more polar; ν_{\max} . (CHCl₃)/cm⁻¹ 2931, 2856, 1668, 1463, 1362, 1128, 870; δ_{H} (400 MHz, CDCl₃) 0.13 (s, 6 H, CH₃), 0.89 (s, 9 H, CH₃), 1.73-1.80 (m, 1 H, CCH_AH_BCH₂), 1.97-2.05 (m, 2 H, CCH_AH_BCH_AH_B), 2.13-2.19 (m, 1 H, CCH₂CH_AH_B), 2.69-2.75 (m, 1 H, ArCH_AH_B), 2.94-3.03 (m, 2 H, CHCHCO, ArCH_AH_B), 3.12 (t, 1 H, *J* 9.6, CHCHCO), 3.29 (ddd, 1 H, *J* 13.2, 10.4, 5.6, NCH_ACH_B), 3.81 (s, 3 H, OCH₃), 3.84 (s, 3 H, OCH₃), 4.15 (m, 1 H, *J* 13.2, 7.2, 3.2, NCH_ACH_B), 4.91 (dd, 1 H, *J* 12.0, 9.6, CH=CHOSi), 5.77-5.81 (m, 1 H, CH=CH), 6.02-6.04 (m, 1 H, CH=CH), 6.37 (d, 1 H, *J* 12.0, CH=CHOSi), 6.59 (s, 1 H, ArH), 6.71 (s, 1 H, ArH); δ_{C} (100 MHz, CDCl₃) -5.2 (SiCH₃), 18.3 (C), 22.1 (CH₂), 25.7 (CH₃), 27.0 (CH₂), 33.4 (CH₂), 35.1 (CH₂), 43.5 (CH), 45.6 (CH), 55.9 (OCH₃), 56.0 (OCH₃), 60.9 (C), 106.7 (CH=CHOSi), 108.2 (ArCH), 111.8 (ArCH), 125.3 (C), 126.9 (CH=), 128.4 (CH=), 133.6 (C), 143.8 (CH=CHOSi), 147.5 (C), 147.9 (C), 174.1 (NC=O); ESIMS *m/z* (%) 456.3 ([M+H]⁺, 100), 478.2 ([M+Na]⁺, 10); HRMS (ESI) found [M+H]⁺, 456.2583. C₂₆H₃₇NO₄Si requires [M+H], 456.2565.

(3*R*,4*R*,4*aS*,5*R*,13*bS*)-3,4-Dibromo-11,12-dimethoxy-5-vinyl-1,2,3,4,4*a*,5,8,9-

octahydroindolo[1-*a*]isoquinolin-6-one **43**

Pyridinium tribromide (64 mg, 0.2 mmol) was added in 6 portions over 2 hours to the solution of imide **21** (240 mg, 0.74 mmol) in CHCl₃ (10 mL) at -20 °C. The resulting solution was then stirred at this temperature for 8 h before warmed to room temperature overnight. The reaction mixture was concentrated *in vacuo* and purified by silica column chromatography (eluent: petroleum ether/EtOAc = 4:1 then 2:1) to give the desired product **43** (43 mg, 45%): pale yellow oil; ν_{\max} (CHCl₃)/cm⁻¹ 2958, 2854, 2253, 1696, 1463, 1359, 1123, 907; δ_{H} (500 MHz, CDCl₃) 1.81-1.86 (m, 1 H), 2.08-2.11 (m, 1 H), 2.24-2.32 (m, 2 H), 2.46-2.53 (m, 1 H, ArCH_AH_B), 3.06 (dd, *J* 9.0, 7.0, 1 H, CHCON), 3.13-3.18 (m, 2 H, NCH_AH_B, ArCH_AH_B), 3.38 (dd, *J* 9.0, 7.0, 1 H, CHCHBr), 3.84 (s, 3 H, OCH₃), 3.92 (s, 3 H, OCH₃), 4.07 (dd, *J* 10.5, 9.0, 1 H, CHBrCH), 4.24-4.36 (m, 2 H, CHBrCH₂, NCH_AH_B), 5.30 (d, *J* 17.0, 1.5, 1 H, CH_AH_B=CH), 5.41 (dd, *J* 10.0, 1.5, 1 H, CH_AH_B=CH), 5.94-6.01 (ddd, *J* 17.0, 10.0, 9.0, 1 H, CH=), 6.52 (s, 1 H, ArH), 6.65 (s, 1 H, ArH); δ_{C} (125 MHz, CDCl₃) 25.3 (CH₂), 32.1 (CH₂), 35.5 (CH₂), 36.5 (CH₂), 50.4 (CH), 53.4 (CH), 56.0 (OCH₃), 56.4 (CH), 56.5 (OCH₃), 56.8 (CH), 63.8 (C), 107.3 (ArCH), 112.5 (ArCH), 121.5 (CH₂=), 126.5 (C), 130.5 (CH=), 130.5 (C), 147.8 (C), 148.7 (C), 177.0 (NC=O); HRMS (ESI) found [M+H]⁺, 484.0117. C₂₀H₂₃Br₂NO₃ requires [*M+H*], 484.0109.

(4a*S*,5*S*,13b*S*)-5-(Hydroxymethyl)-11,12-dimethoxy-1,2,4a,5,8,9-hexahydroindolo[1-*a*]isoquinolin-6-one **44**

A solution of dibromide **43** (60 mg, 0.12 mmol) in CH₂Cl₂ (10 mL) was cooled to -78 °C. A stream of ozone was passed into the solution until the reaction was completed. The excess of ozone was removed by a stream of nitrogen. Acetic acid (1.5 mL) and zinc powder (600 mg) was added. The

reaction mixture was stirred vigorously at reflux for two hours. When the ozonide was completely decomposed and dehalogenated, the reaction mixture was filtered and the zinc powder was washed thoroughly and successively with cold methanol and CH₂Cl₂. The filtrate was washed with saturated aqueous NaHCO₃ solution (10 mL), water (10 mL) and brine (10 mL). The organic phase was dried over MgSO₄ and concentrated *in vacuo*. The crude product was purified by silica column chromatography (eluent: petroleum ether/AcOEt = 1/1) to give the product **44** (40 mg, 97%): colourless oil; ν_{max} . (CHCl₃)/cm⁻¹ 3606, 3455, 2929, 2855, 2253, 1699, 1668, 1463, 1364, 902; δ_{H} (500 MHz, CDCl₃) 1.65-1.71 (m, 1 H, CCH_AH_BCH₂), 2.01-2.06 (m, 2 H, CCH_AH_BCH_AH_B), 2.19-2.23 (m, 1 H, CCH₂CH_AH_B), 2.57-2.63 (m, 2 H, CHCHCO, ArCH_AH_B), 2.84-2.92 (m, 2 H, CHCHCO, ArCH_AH_B), 3.37-3.43 (m, 1 H, NCH_AH_B), 3.76-3.80 (m, 1 H, CH_AH_BOH), 3.76 (s, 3 H, OCH₃), 3.84 (s, 3 H, OCH₃), 3.89 (s, 1 H, OH), 3.96-4.02 (m, 2 H, NCH_ACH_B, CH_AH_BOH), 6.02-6.07 (m, 2H, CH=CH), 6.62 (s, 1 H, ArH), 6.73 (s, 1 H, ArH); δ_{C} (100 MHz, CDCl₃) 22.9 (CH₂), 27.2 (CH₂), 31.9 (CH₂), 35.2 (CH₂), 42.2 (CH), 50.8 (CH), 55.9 (OCH₃), 56.0 (OCH₃), 59.8 (C), 61.5 (CH₂), 107.9 (CH), 111.6 (CH), 125.0 (C), 127.9 (CH), 128.4 (CH), 133.0 (C), 147.7 (C), 148.0 (C), 173.020 (C=O); ESIMS m/z (%) 352.1 ([M+Na]⁺, 100); HRMS (ESI) found [M+H]⁺, 330.1686. C₁₉H₂₃NO₄ requires [M+H], 330.1684.

(4S)-1-(3,4-Dimethoxyphenethyl)-5-(but-3-enyl)-4,5-dihydroxypyrrolidin-2-one 56

Mg turnings (2.2 g, 90 mmol) were placed in a 250 mL three-necked round bottom flask charged with condenser and addition funnel, and then freshly distilled THF (30 mL) was added. 4-Bromo-1-butene (8 mL, 75 mmol) in THF (50 mL) was placed in the funnel and about 5 mL was added in one portion. The resulting reaction mixture was heated to initiate the reaction. The

4-bromo-1-butene solution was added dropwise to maintain gentle reflux. After the addition, the reaction mixture was stirred for another 1 hour at 65 °C then cooled to room temperature. At -78 °C, the above prepared Grignard reagent was added dropwise by cannula to the solution of lactam **54** (4.8 g, 15 mmol) in THF (60 mL). After the addition, the reaction mixture was stirred at same temperature for 4 hours then allowed to warm to rt. Saturated aqueous NH₄Cl solution (10 mL) was added carefully and diluted with EtOAc (200 mL). The combined organic phase was washed with water (20 mL) and brine (20 mL), then dried over MgSO₄ and concentrated *in vacuo*. The crude product was purified by silica column chromatography (eluent: petroleum ether/AcOEt = 1/1) to give the partially separable diol **56** as a mixture of diastereoisomers with a ratio of 3:1 (3.1g, 61%). Major diastereoisomer: colourless oil; $[\alpha]_D^{25} -204$ (*c* 0.95, CHCl₃); ν_{\max} (CHCl₃)/cm⁻¹ 3612, 3506, 2938, 2838, 1710, 1682, 1455, 1362, 1142; δ_H (400 MHz, *d*-acetone) 1.63-1.75 (m, 1 H, CCH_AH_B), 1.85-2.00 (m, 1 H, CCH_AH_B), 2.02-2.20 (m, 2 H, CH₂CH=), 2.25 (dd, *J* 17.2, 3.2, 1 H, NCOCH₄H_B), 2.62 (dd, *J* 17.2, 6.8, 1 H, NCOCH_AH_B), 2.75-2.95 (m, 2 H, ArCH₂), 3.25 (m, 1 H, NCH_AH_B), 3.50 (m, 1 H, NCH_AH_B), 3.76 (s, 3 H, OCH₃), 3.80 (s, 3 H, OCH₃), 4.30 (dd, *J* 6.8, 3.2, 1 H, CHOH), 4.56 (s, 1 H, OH), 4.93 (s, 1 H, OH), 4.94 (dd, *J* 10.0, 2.0, 1 H, CH_AH_B=), 5.04 (dd, *J* 17.2, 2.0, 1 H, CH_AH_B=), 5.83-5.90 (m, 1 H, CH=CH₂), 6.60-6.80 (m, 3H, ArH); δ_C (100.6 MHz, *d*-acetone) 28.8 (CH₂CH=), 35.7 (ArCH₂), 36.7 (COHCH₂), 39.5 (NCOCH₂), 41.8 (NCH₂), 56.1 (OCH₃), 56.2 (OCH₃), 69.1 (CHOH), 91.7 (COH), 113.0 (ArCH), 113.7 (ArCH), 115.0 (CH₂=), 121.6 (ArCH), 133.4 (ArC), 139.0 (CH=), 148.9 (ArC), 150.4 (ArC), 170.0 (C=O); ESIMS *m/z* (%) 358.2 ([M+Na]⁺, 83), 336.18 ([M+H]⁺, 91), 318.2 ([M-H₂O]⁺, 100); HRMS (ESI) found [M+H]⁺, 336.1792. C₁₈H₂₅NO₅ requires [M+H], 336.1793.

(1S,10bR)-10b-(But-3-enyl)-8,9-dimethoxy-3-oxo-1,2,3,5,6,10b-hexahdropyrro-

1o[2,1-*a*]isoquinolin-1-yl acetate **57**

Acetic anhydride (229 mg, 2.2 mmol), triethylamine (252 mg, 2.5 mmol) and *N,N*-4-dimethylaminopyridine (12 mg, 0.1 mmol) were added to a solution of alcohol **56** (335 mg, 1 mmol) in CH₂Cl₂ (6 mL) at 0 °C. The resulting mixture was stirred at room temperature for 4 hours until the reaction was completed. The reaction mixture was then extracted with CH₂Cl₂ (100 mL). The organic phase was washed with water (10 mL), brine (10 mL), then dried over MgSO₄ and concentrated *in vacuo*. The crude product was dissolved in CH₂Cl₂ (10 mL) and BF₃·OEt₂ (284 mg, 2 mmol) was added at -78 °C. The reaction mixture was stirred at the same temperature for 2 hours, then warmed to room temperature overnight before addition of water (5 mL). The mixture was then extracted with CH₂Cl₂ (50 mL), the organic phase was washed with saturated aqueous NaHCO₃ solution (10 mL), water (10 mL) and brine (10 mL), then dried over MgSO₄ and concentrated *in vacuo*. The crude product was purified by silica column chromatography (eluent: petroleum/AcOEt = 1/1) to give a mixture of 3:1 diastereoisomers (305 mg, 85%). Major product **57**: [α]_D²⁵ -243 (c = 1/1), CHCl₃); ν_{max.} (CHCl₃)/cm⁻¹ 2937, 2253, 1744, 1687, 1463, 898; δ_H (400 MHz, CDCl₃) 1.90-2.10 (m, 4 H, 2CH₂), 2.20 (s, 3 H, COCH₃), 2.50-2.60 (ddd, *J* 17.0, 8.7, 1.2, 1 H, CH_AH_BCON), 2.60-2.70 (dd, *J* 17.0, 3.7, 1 H, ArCH_AH_B), 2.82-2.90 (m, 1 H, ArCH_AH_B), 2.92 (dd, *J* 17.0, 9.0, 1 H, CH_AH_BCON), 3.01-3.12 (m, 1H, NCH_AH_B), 3.83 (s, 3 H, OCH₃), 3.88 (s, 3 H, OCH₃), 4.42 (ddd, *J* 13.0, 6.5, 1.2, 1 H, NCH_AH_B), 5.00 (m, 2 H, CH₂=CH), 5.30 (dd, *J* 9.0, 3.7, 1 H, CHOAc), 5.70-5.80 (m, 1 H, CH=CH₂), 6.57 (s, 1 H, ArH), 6.68 (s, 1 H, ArH); δ_C (100.6 MHz, CDCl₃) 21.2 (CH₃), 27.9 (CH₂), 29.1 (CH₂), 35.2 (CH₂), 36.6 (NCOCH₂), 37.8 (NCH₂), 55.9 (OCH₃), 56.0 (OCH₃), 65.2 (C), 75.7 (CH), 107.5 (ArCH), 111.6 (ArCH), 115.2 (CH₂=), 124.9 (ArC), 131.8 (ArC), 137.6 (CH=), 148.1 (ArC), 148.3 (ArC), 169.5 (NC=O), 170.0 (MeC=O);

ESIMS m/z (%) 360.2 ($[M+H]^+$, 59), 382.2 ($[M+Na]^+$, 100); HRMS (ESI) found $[M+H]^+$, 360.1805.

$C_{20}H_{25}NO_5$ requires $[M+H]$, 360.1804.

(S)-10b-(But-3-enyl)-8,9-dimethoxy-5,6-dihydropyrrolo[2,1-*a*]isoquinolin-3-one (-)-58

To a stirred solution of NaH (2.6 g, 64 mmol, 60% dispersion in mineral oil) in THF (20 mL) was added dropwise a solution of mixture **57** (1.6 g, 4.3 mmol) in THF (10 mL). The resulting solution was then stirred overnight under nitrogen atmosphere. The reaction mixture was added dropwise to the ice-water and extracted with EtOAc (200 mL). The organic phase was washed with water (10 mL), brine (10 mL), dried over $MgSO_4$ and concentrated *in vacuo*. The crude product was purified by silica column chromatography (eluent: petroleum ether /AcOEt = 2/1) to give a viscous yellow oil (-)-**58** (1.2 g, 95%): $[\alpha]_D^{25}$ -108 (c 2.20, $CHCl_3$); ν_{max} . ($CHCl_3$)/ cm^{-1} 2937, 2847, 2936, 1681, 1360, 1108; δ_H (400 MHz, $CDCl_3$) 1.86-1.95 (m, 2 H, CCH_2), 2.01-2.10 (m, 2 H, $CH_2CH=$), 2.67 (dd, J 16.1, 4.0, 1 H, $ArCH_AH_B$), 2.94 (ddd, J 16.1, 12.0, 6.6, 1 H, $ArCH_AH_B$), 3.18 (ddd, 1 H, J 13.3, 12.0, 4.0, NCH_AH_B), 3.83 (s, 3 H, OCH_3), 3.88 (s, 3 H, OCH_3), 4.40 (dd, J 13.3, 6.6, 1 H, NCH_AH_B), 5.00 (m, 2 H, $CH_2=$), 5.70-5.80 (m, 1 H, $CH=CH_2$), 6.18 (d, J 5.8 Hz, 1H, $CH=$), 6.60 (s, 1 H, ArH), 6.70 (s, 1 H, ArH), 7.29 (d, J 5.8, 1 H, $CH=$); δ_C (100 MHz, $CDCl_3$) 27.6 (CH_2), 29.1 (CH_2), 34.8 (CH_2), 37.9 (NCH_2), 56.0 (OCH_3), 56.3 (OCH_3), 68.4 (C), 109.2 ($CH=$), 112.2 ($CH=$), 115.2 ($CH_2=$), 125.3 (ArC), 126.4 ($CH=$), 129.4 (ArC), 137.5 ($CH=$), 147.7 (ArC), 148.3 (ArC), 151.7 ($CH=$), 170.9 ($C=O$); ESIMS m/z (%) 322.1 ($[M+Na]^+$, 100), 300.2 ($[M+H]^+$, 76); HRMS (ESI) found M^+ , 299.1522. $C_{18}H_{21}NO_3$ requires M , 299.1521; The ee was determined as 47% by HPLC (Chiracel OD Column, 20% i PrOH in hexane, 0.4 mL/min); the retention times were 23.4 min (minor) and 31.2 min (major).

(4S)-1-(3,4-Dimethoxyphenethyl)-5-(but-3-enyl)-5-hydroxy-4-(triisopropylsilyloxy)pyrrolidin-2-one 59

To a solution of hydroxyl lactam **56** (1.8 g, 5.4 mmol, a 3:1 mixture of diastereomers) in CH₂Cl₂ (15 mL) was added 2,6-lutidine (1.2 mL, 10.7 mmol) and TIPSOTf (2.2 mL, 8 mmol). The resulting reaction mixture was then stirred at room temperature for 8 hours before dilution with CH₂Cl₂ (100 mL). The organic phase was washed with saturated aqueous NaHCO₃ (10 mL), H₂O (10 mL) and brine (10 mL). The organic phase was dried over MgSO₄ and concentrated *in vacuo*. The crude product was purified by silica chromatography (eluent: petroleum ether/AcOEt = 5/1 to 2/1) to give the hydroxylactam **59** (2.3 g, 88%) as a mixture of diastereoisomers in a ratio of 3:1. Major diastereoisomer: colourless oil; less polar; $[\alpha]_D^{31} +12$ (*c* 2.37, CHCl₃); ν_{\max} . (CHCl₃)/cm⁻¹ 3487, 2943, 2866, 1682, 1463, 1352, 1096, 883; δ_H (400 MHz, *d*-acetone) 1.03-1.24 (m, 21 H, SiCH(CH₃)₂), 1.70-1.91 (m, 2 H, CH₂COH), 1.94-2.21 (m, 2 H, CH₂CH=), 2.30 (dd, *J* 16.8, 2.4, 1 H, CH_AH_BCO), 2.75 (dd, *J* 16.8, 6.0, 1 H, CH_AH_BCO), 2.80-2.91 (m, 2 H, ArCH₂), 3.18-3.29 (m, 1 H, NCH_AH_B), 3.48-3.53 (m, 1 H, NCH_AH_B), 3.79 (s, 3 H, OCH₃), 3.82 (s, 3 H, OCH₃), 4.06 (s, 1 H, OH), 4.51 (dd, *J* 6.0, 2.4, 1 H, CHOTIPS), 4.97 (dd, 1 H, *J* 6.0, 2.0, CH_AH_B=CH), 5.04 (dd, 1 H, *J* 17.2, 2.0, CH_AH_B=CH), 5.78-5.88 (m, 1 H, CH₂=CH), 6.76-7.01 (m, 3 H, ArH); δ_C (100 MHz, CDCl₃) 13.0 (CHSi), 18.4 (CH₃), 24.5 (CH₂COH), 35.9 (ArCH₂), 36.3 (CH₂CH=), 40.6 (CH₂CO), 41.7 (NCH₂), 56.1 (OCH₃), 71.2 (CHOSi), 95.0 (COH), 112.9 (ArCH), 113.7 (ArCH), 115.2 (CH₂=), 121.5 (ArCH), 133.2 (ArC), 138.8 (CH=), 148.9 (ArC), 150.4 (ArC), 171.2 (NC=O); ESIMS *m/z* (%) 474.3 ([M-H₂O]⁺, 57), 492.3 ([M+H]⁺, 100), 514.3 ([M+Na]⁺, 48); HRMS (ESI) found [M+H]⁺, 492.3140. C₂₇H₄₅NO₅Si requires [M+H], 492.3150. Minor diastereoisomer: colourless oil; more polar; δ_H (400 MHz, *d*-acetone) 1.03-1.24 (m, 21 H, SiCH(CH₃)₂), 1.72-2.04

(m, 3 H, $CCH_2CH_AH_B$), 2.23-2.39 (m, 2 H, $CCH_2CH_AH_B$, CH_AH_BCON), 2.74 (dd, J 16.7, 8.0, 1 H, CH_AH_BCON), 2.79-2.86 (m, 1 H, $ArCH_AH_B$), 2.96 (ddd, J 13.2, 9.1, 7.5, 1 H, $ArCH_AH_B$), 3.20 (ddd, J 13.5, 9.1, 7.5, 1 H, NCH_AH_B), 3.65 (ddd, J 13.5, 9.3, 4.7, 1 H, NCH_AH_B), 3.83 (s, 3 H, OCH_3), 3.86 (s, 3 H, OCH_3), 4.22 (t, 1 H, J 8.0, $CHOSi$), 4.95 (dd, 1 H, J 6.0, 2.0, $CH_AH_B=CH$), 4.99 (dd, 1 H, J 17.2, 2.0, $CH_AH_B=CH$), 5.70-5.80 (m, 1 H, $CH_2=CH$), 6.72-6.80 (m, 3 H, ArH); δ_C (100 MHz, $CDCl_3$) 12.2 ($CHSi$), 17.9 (CH_3), 27.8 (CH_2COH), 33.9 ($ArCH_2$), 34.4 ($CH_2CH=$), 40.1 (CH_2CO), 41.4 (NCH_2), 55.9 (OCH_3), 77.1 ($CHOSi$), 94.4 (COH), 111.3 ($ArCH$), 112.2 ($ArCH$), 115.0 ($CH_2=$), 120.8 ($ArCH$), 131.8 (ArC), 137.5 ($CH=$), 147.7 (ArC), 149.0 (ArC), 171.0 ($NC=O$); HRMS (ESI) found $[M+H]^+$, 492.3131. $C_{27}H_{45}NO_5Si$ requires $[M+H]$, 492.3145.

(1*S*,10*bS*)-10*b*-(3-Butenyl)-8,9-dimethoxy-1-(triisopropylsilyloxy)-1,2,5,6-tetrahydropyrrolo[2,1-*a*]isoquinolin-3-one **60 and minor diastereomer **61****

The protected hydroxy lactam **59** as a mixture of diastereomers in a ratio of 3:1 (2.9 g, 6 mmol) in CH_2Cl_2 (30 mL) was treated with $BF_3 \cdot Et_2O$ (3.8 mL, 29 mmol) at -78 °C. The resulting reaction mixture was stirred at this temperature for 2 hours then warmed to rt overnight. The reaction mixture was then extracted with CH_2Cl_2 (100 mL). The organic phase was washed with water (10 mL) and brine (10 mL). The organic phase was dried over $MgSO_4$ and concentrated *in vacuo*. The crude product was purified on silica column (eluent: petroleum ether/ $AcOEt$: 6:1 to 4:1) to give the major product **60** (2.6 g, 91%) and the other minor diastereoisomer **61** (147 mg, 2%). Major product **60**: colourless solid; less polar; mp 101-103 °C; $[\alpha]_D^{25}$ +133 (c 0.80, $CHCl_3$); ν_{max} ($CHCl_3$)/ cm^{-1} 2943, 2866, 1678, 1463, 1102, 883; δ_H (500 MHz, $CDCl_3$) 0.81-0.87 (m, 21 H, $3CH(CH_3)_2$), 1.85-2.05 (m, 4 H, CH_2CH_2), 2.37 (d, J 17.0, 1 H, $ArCH_AH_B$), 2.60 (dd, J 15.0, 3.0,

1 H, CH_AH_BCON), 2.72-2.78 (m, 1 H, $ArCH_AH_B$), 2.95-3.04 (m, 2 H, NCH_AH_B , CH_AH_BCON), 3.84 (s, 3 H, OCH_3), 3.85 (s, 3 H, OCH_3), 4.45-4.49 (m, 2 H, NCH_AH_B , $CHOTIPS$), 4.93 (m, 2 H, $CH_2=CH$), 5.64-5.71 (m, 1 H, $CH=CH_2$), 6.58 (s, 1 H, ArH), 6.64 (s, 1 H, ArH); δ_C (125 MHz, $CDCl_3$) 12.7 (CH), 17.8 (CH_3), 17.9 (CH_3), 29.1 (CH_2), 29.4 (CH_2), 37.6 (CH_2), 39.6 (CH_2), 41.9 (NCH_2), 56.0 (OCH_3), 70.7 (C), 76.3 (CH), 109.0 ($ArCH$), 111.8 ($ArCH$), 115.2 ($CH_2=$), 127.3 (ArC), 128.8 (ArC), 137.7 ($CH=$), 147.8 (ArC), 147.9 (ArC), 172.5 ($NC=O$); ESIMS m/z (%) 474.3 ($[M+H]^+$, 100), 496.3 ($[M+Na]^+$, 39); HRMS (ESI) found $[M+H]^+$, 474.3034. $C_{27}H_{43}NO_4Si$ requires $[M+H]$, 474.3064. Minor product **61**: colourless oil; more polar; $[\alpha]_D^{23}$ -161 (c 0.70, $CHCl_3$); ν_{max} ($CHCl_3$)/ cm^{-1} 2945, 2868, 1678, 1462, 1110, 883; δ_H (400 MHz, $CDCl_3$) 1.08-1.16 (m, 21 H, $CH(CH_3)_2$), 1.93-2.03 (m, 2 H, CH_2), 2.16-2.32 (m, 2 H, CH_2), 2.62-2.72 (m, 3 H, $ArCH_2$, CH_AH_BCON), 2.80-2.89 (m, 1 H, CH_AH_BCON), 2.98 (td, J 12.4, 4.0, 1 H, CH_AH_BN), 3.86 (s, 6 H, OCH_3), 4.42-4.50 (m, 2 H, CH_AH_BN , $CHOTIPS$), 4.92-5.00 (m, 2 H, $CH_2=CH$), 5.71-5.78 (m, 1 H, $CH=$), 6.56 (s, 1 H, ArH), 6.93 (s, 1 H, ArH); δ_C (100 MHz, $CDCl_3$) 12.7 (SiCH), 18.2 (CH_3), 28.6 (CH_2), 29.3 (CH_2), 35.2 (CH_2), 36.0 (CH_2), 40.8 (NCH_2), 55.9 (OCH_3), 56.0 (OCH_3), 76.3 ($CHOSi$), 108.1 ($ArCH$), 111.6 ($ArCH$), 114.8 ($CH_2=$), 124.8 (ArC), 133.0 (ArC), 138.1 ($CH=$), 147.9 (ArC), 148.0 (ArC), 169.8 ($NC=O$); ESIMS m/z (%) 474.3 ($[M+H]^+$, 77), 496.3 ($[M+Na]^+$, 100); HRMS (ESI) found $[M+H]^+$, 474.3022. $C_{27}H_{43}NO_4Si$ requires $[M+H]$, 474.3040.

(R)-10b-(3-Butenyl)-8,9-dimethoxy-5,6-dihydropyrrolo[2,1-a]isoquinolin-3-one (+)-58

TBAF (0.2 mL, 0.2 mmol, 1 M in THF) was added to the solution of lactam **60** (65 mg, 0.14 mmol) in THF (2 mL). The resulting reaction mixture was then stirred at rt for 3 h. The mixture was

extracted with EtOAc (50 mL), the organic phase was washed with H₂O (10 mL), brine (10 mL), then dried over MgSO₄ and concentrated *in vacuo*. The crude product was purified by silica chromatography (eluent: petroleum ether/AcOEt = 2/1 then pure EtOAc) gave the alcohol corresponding to **60** (39 mg, 91%) as a colorless oil: $[\alpha]_D^{25} +182$ (*c* 1.89, CHCl₃);

Et₃N (76 mg, 0.75 mmol), Ac₂O (55 mg, 0.53 mmol) and DMAP (6.0 mg, 0.05 mmol) were added to the solution of secondary alcohol (160 mg, 0.5 mmol) in CH₂Cl₂ (4 mL). The resulting solution was then stirred at rt for 4 h. The reaction mixture was then extracted with Et₂O (100 mL). The organic phase was washed with water (10 mL), brine (10 mL), then dried over MgSO₄ and concentrated *in vacuo*. The crude product was purified by silica chromatography (eluent: petroleum ether/AcOEt = 1/1) to give the acetate corresponding to **60** (130 mg, 78%) as a colourless oil: $[\alpha]_D^{25} +112$ (*c* 0.85, CHCl₃); ν_{\max} . (CHCl₃)/cm⁻¹ 2938, 2836, 1738, 1682, 1463, 1363, 1042, 907; δ_H (400 MHz, CDCl₃) 1.58 (s, 3 H, COCH₃), 1.92-2.14 (m, 4 H, CH₂CH₂), 2.38 (d, *J* 17.6, 1 H, CH_AH_BPh), 2.65 (dd, *J* 15.6, 3.2, 1 H, CH_AH_BCON), 2.80-2.88 (m, 1 H, CH_AH_BPh), 3.00-3.11 (m, 2 H, CH_AH_BCON, CH_AH_BN), 3.83 (s, 3 H, OCH₃), 3.87 (s, 3 H, OCH₃), 4.44 (dd, *J* 13.2, 5.6, 1 H, CH_AH_BN), 4.95-5.01 (m, 2 H, CH=CH₂), 5.67-5.73 (m, 2 H, CH=CH₂, CHOAc), 6.51 (s, 1 H, ArH), 6.59 (s, 1 H, ArH); δ_C (100 MHz, CDCl₃) 20.7 (CH₃), 28.6 (CH₂), 28.8 (CH₂), 36.4 (CH₂), 38.6 (CH₂), 39.8 (NCH₂), 55.8 (OCH₃), 56.0 (OCH₃), 68.6 (C), 73.4 (CH), 108.8 (ArCH), 111.4 (ArCH), 115.5 (CH₂=), 126.5 (ArC), 127.1 (ArC), 137.0 (CH=), 147.4 (ArC), 147.8 (ArC), 169.9 (NC=O), 171.0 (C=O); ESIMS *m/z* (%) 382.2 ([M+Na]⁺, 100); HRMS (ESI) found [M+H]⁺, 360.1803. C₂₀H₂₅NO₅ requires [M+H], 360.1811.

To a stirred solution of NaH (2.6 g, 64 mmol, 60% dispersion in mineral oil) in THF (20 mL) was

added dropwise a solution of acetate (1.6 g, 4.3 mmol) in THF (10 mL). The resulting solution was then stirred overnight under a nitrogen atmosphere. The reaction mixture was added dropwise to ice-water and extracted with EtOAc (200 mL). The organic phase was washed with water (10 mL), brine (10 mL), dried over MgSO₄ and concentrated *in vacuo*. The crude product was purified by silica column chromatography (eluent: petroleum ether/AcOEt = 2/1) to give a viscous yellow oil (+)-**58** (1.2 g, 95%): [α]_D²⁷ +242 (*c* 1.57, CHCl₃). The spectral data were identical with (-)-**58**. The ee was determined as >99% by HPLC (Chiracel OD Column, 20% ⁱPrOH in hexane, 0.4 mL/min); the retention time was 23.4 min (major) and 31.2 min (minor).

(1S,10bR)-8,9-Dimethoxy-3-oxo-1,2,5,6-tetrahydropyrrolo[2,1-*a*]-isoquinolin-1-yl acetate 67

NaBH₄ (38 mg, 1.0 mmol) was added to the solution of imide **54** (321 mg, 1.0 mmol) in MeOH (2 mL) and CH₂Cl₂ (2 mL) at -40 °C, the resulting solution was stirred for 4 h. The mixture was quenched with water (2 mL) and diluted with CH₂Cl₂ (50 mL). The organic phase was washed with H₂O (5 mL), brine (5 mL), dried over anhydrous MgSO₄ and concentrated *in vacuo* to give a white solid which was dissolved in CH₂Cl₂ (4 mL) at 0 °C. BF₃-Et₂O (0.6 mL, 4.4 mmol) was added and the resulting solution was stirred at 0 °C for 6 h and then at rt for one day. The mixture was extracted with CH₂Cl₂ (50 mL). The organic phase was washed with water (10 mL), brine (10 mL), dried over MgSO₄ and concentrated *in vacuo*. The crude product was purified by flash column chromatography (eluent: petroleum ether/AcOEt = 1:1) to give **67** as a white foam (160 mg, 56% for two steps) as a single diastereoisomer: mp 99-101 °C; [α]_D²¹ -94 (*c* 2.20, CHCl₃); ν_{\max} (CHCl₃)/cm⁻¹ 2937, 2836, 1738, 1683, 1613, 1456, 1363, 1114, 1041, 998; δ_{H} (400 MHz, CDCl₃) 2.12 (s, 3 H, CH₃), 2.52-2.61 (m, 2 H, ArCH_AH_B, CH_AH_BCON), 2.85-2.95 (m, 2 H, ArCH_AH_B,

CH_AH_BCON), 3.03 (td, *J* 12.5, 4.0, 1H, CH_AH_BN), 3.84 (s, 3 H, OCH₃), 3.86 (s, 3 H, OCH₃), 4.34 (ddd, *J* 12.5, 6.5, 1.5, 1 H, CH_AH_BN), 4.72 (d, *J* 4.0, 1 H, CHCHOAc), 5.23-5.27 (m, 1 H, CHOAc), 6.57 (s, 1 H, ArH), 6.98 (s, 1 H, ArH); δ_C (100 MHz, CDCl₃) 12.1 (CH₃), 27.5 (ArCH₂), 37.4 (NCH₂), 37.8 (COCH₂), 55.9 (OCH₃), 62.8 (NCH), 73.8 (CHOAc), 107.9 (ArCH), 111.7 (ArCH), 125.6 (ArCH), 126.1 (ArC), 148.1 (ArC), 148.4 (ArC), 170.56 (C=O), 170.59 (C=O); ESIMS *m/z* (%) 306.1 ([M+H]⁺, 35), 328.1 ([M+Na]⁺, 100); HRMS (ESI) found [M+H]⁺, 306.1325. C₁₆H₁₉NO₅ requires [*M+H*], 306.1342.

(S)-1-(3,4-Dimethoxyphenethyl)-3-(triisopropylsilyloxy)pyrrolidine-2,5-dione 64

To a solution of acetate **54** (1.6 g, 5.0 mmol) in absolute ethanol (30 mL) was added dropwise acetyl chloride (12 mL). The mixture was stirred at 50 °C for 5 h and concentrated *in vacuo*. The mixture was then extracted with CH₂Cl₂ (100 mL). The organic phase was washed with saturated aqueous NaHCO₃ (10 mL), followed by water (10 mL) then brine (10 mL), dried (MgSO₄), filtered and concentrated *in vacuo* to give a white solid **63** (1.2 g, 86%). To a solution of imide **63** (558 mg, 2.0 mmol) in CH₂Cl₂ (10 mL) at 0 °C was added 2, 6-lutidine (0.5 mL, 4.0 mmol), and TIPSOTf (0.8 mL, 3.0 mmol) dropwise. The resulting reaction mixture was stirred at rt until the reaction was complete. The mixture was extracted with CH₂Cl₂ (50 mL). The organic phase was washed with 1 M HCl (10 mL), followed by water (10 mL) then brine (10 mL), dried (MgSO₄) and concentrated *in vacuo* to give a pure yellow oil **64** which was used for the next step without further purification: [α]_D²¹ -32 (*c* 2.80, CHCl₃); ν_{max.} (CHCl₃)/cm⁻¹ 2944, 2868, 2839, 1592, 1463, 1351, 1140, 883; δ_H (400 MHz, CDCl₃) 1.06-1.13 (m, 21 H, SiCH(CH₃)₂), 2.57 (dd, *J* 18.0, 5.0, 1 H, CH_AH_BCON), 2.85 (t, *J* 8.0, 2 H, ArCH₂), 2.98 (dd, *J* 18.0, 8.0, 1 H, CH_AH_BCON), 3.72 (dd, *J* 9.0, 6.5, 1 H, CH_AH_BN), 3.85 (s, 3 H, OCH₃), 3.87 (s, 3 H, OCH₃), 4.63 (dd, *J* 8.0, 5.0, 1 H, CHOSi), 6.73-6.79 (m, 3 H,

ArH); δ_C (100.6 MHz, CDCl₃) 12.1 (CH), 18.1 (CH₃), 32.9 (ArCH₂), 39.8 (NCH₂), 40.0 (NCOCH₂), 55.8 (OCH₃), 68.1 (CHOSi), 111.2 (ArCH), 111.9 (ArCH), 121.0 (ArCH), 129.9 (ArC), 147.8 (ArC), 149.0 (ArC), 173.9 (C=O), 176.5 (C=O); ESIMS *m/z* (%) 436.2 ([M+H]⁺, 35), 458.2 ([M+Na]⁺, 100); HRMS (ESI) found [M+H]⁺, 436.2518. C₂₃H₃₇NO₅Si requires [M+H], 436.2514.

(1S,10bR)-8,9-Dimethoxy-1-(triisopropylsilyloxy)-1,2,5,6-tetrahydropyrrolo[2,1-a]isoquinolin-3-one 68

The crude imide **64** was dissolved in MeOH (6 mL) at -40 °C, and NaBH₄ (76 mg, 2.0 mmol) was added. The resulting solution was stirred until the reaction was completed. The reaction was quenched with water (2 mL), then extracted with CH₂Cl₂ (50 mL), washed with H₂O (10 mL) and brine (10 mL). The organic phase was dried over anhydrous MgSO₄ and concentrated *in vacuo*. The crude product was dissolved in CH₂Cl₂ (8 mL) and BF₃·Et₂O (1.5 mL, 12 mmol) was added at -40 °C. The resulting solution was then allowed to warm to room temperature slowly before dilution with CH₂Cl₂ (50 mL). The organic phase was washed with water (10 mL), brine (10 mL), dried over MgSO₄ and concentrated *in vacuo*. The crude product was purified by flash silica chromatography (eluent: petroleum ether/AcOEt = 1:1) gave the major product **68** (312 mg) as a colourless solid and the other minor diastereoisomer **70** (62 mg) with a 47% yield for three steps. Major product **68**: white solid; less polar; mp 99-102 °C; $[\alpha]_D^{20}$ -87 (*c* 2.80, CHCl₃); ν_{\max} . (CHCl₃)/cm⁻¹ 2943, 2867, 1683, 1613, 1461, 1363, 1132, 1089, 996, 883; δ_H (400 MHz, CDCl₃) 1.04-1.16 (m, 21 H, SiCH(CH₃)₂), 2.59-2.94 (m, 5 H, NCH_AH_B, ArCH₂, CH₂CON), 3.85 (s, 3 H, OCH₃), 3.86 (s, 3 H, OCH₃), 4.33-4.39 (m, 2 H, NCH_AH_B, CHOTIPS), 4.56 (d, *J* 6.4, 1 H, CHCHOTIPS), 6.60 (s, 1 H, ArH), 6.99(s, 1 H, ArH); δ_C (100 MHz, CDCl₃) 12.5 (SiCH), 18.1 (CH₃), 28.4 (ArCH₂), 36.5 (NCH₂), 41.8 (NCOCH₂), 55.8 (OCH₃), 64.0 (NCH), 74.9 (CHOSi),

108.2 (ArCH), 111.6 (ArCH), 125.7 (ArC), 127.0 (ArC), 147.8 (ArC), 148.0 (ArC), 170.0 (NC=O); ESIMS m/z (%) 420.3 ($[M+H]^+$, 62), 442.2 ($[M+Na]^+$, 100); HRMS (ESI) found $[M+H]^+$, 420.2565. $C_{23}H_{37}NO_4Si$ requires $[M+H]$, 420.2570. Minor product **70**: oil; more polar; $[\alpha]_D^{23} +112$ (c 2.80, $CHCl_3$); ν_{max} . ($CHCl_3$)/ cm^{-1} 2943, 2867, 1683, 1604, 1464, 1364, 1120, 883; δ_H (400 MHz, $CDCl_3$) 0.81-1.18 (m, 21 H, $SiCH(CH_3)_2$), 2.49 (d, J 16.0, 1 H, $NCOCH_AH_B$), 2.62 (dd, J 16.0, 2.0, 1 H, $ArCH_AH_B$), 2.70-2.89 (m, 3 H, $ArCH_AH_B$, NCH_AH_B , $COCH_AH_B$), 3.86 (s, 3 H, OCH_3), 3.87 (s, 3 H, OCH_3), 4.42 (ddd, J 12.5, 5.5, 1.5, 1 H, CH_AH_BN), 4.80 -4.83 (m, 2 H, $CHCHOTIPS$), 6.63 (s, 2 H, ArH); δ_C (100.6 MHz, $CDCl_3$) 12.5 (SiCH), 17.7 (CH_3), 17.8 (CH_3), 29.0 (ArCH₂), 37.2 (NCH₂), 43.2 (NCOCH₂), 55.8 (OCH_3), 56.1 (OCH_3), 63.8 (NCH), 71.2 (CHOSi), 109.1 (ArCH), 112.0 (ArCH), 124.1 (ArC), 128.4 (ArC), 147.9 (ArC), 147.9 (ArC), 172.2 (C=O); ESIMS m/z (%) 420.2 ($[M+H]^+$, 58), 442.2 ($[M+Na]^+$, 100); HRMS (ESI) found $[M+H]^+$, 420.2573. $C_{23}H_{37}NO_4Si$ requires $[M+H]$, 420.2570.

(R)-10b-(3-Hydroxy-4-(phenylselanyl)butyl-8,9-dimethoxy-5,6-dihydropyrrolo-[2,1-a]isoquinolin-3-one 72

Lactam (+)-**58** (73 mg, 0.24 mmol) was dissolved in the mixture of CH_3CN (4 mL) and water (1 mL). A solution of PhSeCl (51 mg, 0.27 mmol) in CH_3CN (1 mL) was then added and the resulting solution was stirred at r.t. overnight. The reaction mixture was diluted with water (2 mL) and extracted with EtOAc (20 mL). The combined organic phase was washed with saturated aqueous Na_2CO_3 solution (5 mL), water (5 mL) and brine (5 mL). The organic phase was then dried over $MgSO_4$ and concentrated *in vacuo*. The crude product was purified by column chromatography (eluent: petroleum ether/AcOEt = 1/2) to give the desired secondary alcohol **72** (100 mg, 88%) as a

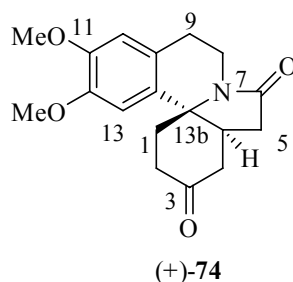
mixture of diastereomers with a ratio of 10:7: ν_{\max} . (CHCl₃)/cm⁻¹ 3518, 2936, 1682, 1362, 1360, 1110; δ_{H} (400 MHz, CDCl₃) 1.20-1.50 (m, 3.3 H, CH₂), 1.90-2.30 (m, 3.3 H, CH₂), 2.90-3.20 (m, 8.5 H, CHHN, CH₂Ar, CH₂SeAr), 3.58 (m, 1.7 H, CHOH), 3.80-3.83 (s, 10 H, OCH₃), 4.34 (dd, *J* 13.2, 6.4, 1.7 H, CHHN), 6.06 (d, *J* 6.0, 1.7 H, CH=), 6.55 (s, 1.7 H, ArH), 6.65 (s, 0.7 H, ArH), 6.68 (s, 1 H, ArH), 7.10-7.30 (m, 6.6 H, ArH, CH=), 7.40-7.50 (m, 3.3 H, ArH); δ_{C} (100 MHz, CDCl₃) 29.8 (CH₂), 29.9 (CH₂), 34.3 (CH₂), 34.6 (CH₂), 34.8 (CH₂), 36.4 (CH₂), 36.8 (CH₂), 55.8 (OCH₃), 56.1 (OCH₃), 68.1 (C), 68.2 (C), 69.3 (CH), 69.6 (CH), 109.1 (CH), 111.9 (CH), 112.0 (CH), 124.9 (C), 125.0 (C), 126.1 (CH), 127.2 (CH), 129.1 (CH), 129.2 (CH), 132.8 (CH), 132.9 (CH), 147.5 (C), 148.0 (C), 151.7 (CH), 151.9 (CH), 170.7 (C=O), 170.8 (C=O); ESIMS *m/z* (%) 496.1 ([M+Na]⁺, 22), 474.1 ([M+H]⁺, 100); HRMS (ESI) found [M+H]⁺, 474.1178. C₂₄H₂₇NO₄Se requires [M+H], 474.1162.

(4aR,13bR)-3-Hydroxy-11,12-dimethoxy-1,2,3,4,4a,5,8,9-octahydroindolo[1-*a*]-isoquinolin-6-one 73

The mixture of secondary alcohols **72** (100 mg, 0.21 mmol) was dissolved in degassed benzene (6 mL). A solution of Ph₃SnH (111 mg, 0.32 mmol) and AIBN (17 mg, 0.1 mmol) in benzene (12 mL) was degassed and was then added to the above solution, at reflux, using a syringe pump, over 8 hours. After the addition the resulting reaction mixture was refluxed for another 4 hours. The reaction was cooled to room temperature and concentrated *in vacuo* to give the crude product which was further purified by silica gel column chromatography (eluent: petroleum ether/AcOEt = 2/1 then pure acetone) to give the cyclized product **73** (51 mg, 85%) as a mixture of diastereoisomers with a ratio of 10:7: colourless oil; ν_{\max} . (CHCl₃)/cm⁻¹ 3605, 2936, 2253, 1682, 1124, 903; δ_{H} (400

MHz, CDCl₃, *major diastereomer*) 1.49-1.61 (m, 2 H, CCH_AH_B, CH_AH_BCOH), 1.67-1.73 (m, 1 H, CH_AH_BCOH), 1.84-1.88 (m, 1 H, CCH_AH_B), 2.12-2.35 (m, 4 H, NCOCH₂, CH_AH_BCOHCH_AH_B), 2.56-2.60 (m, 1 H, ArCH_AH_B), 2.67-2.69 (m, 1 H), 3.03-3.10 (m, 1 H, ArCH_AH_B), 3.17-3.25 (m, 1 H, CH_AH_BN), 3.83 (s, 3 H, OCH₃), 3.86 (s, 3 H, OCH₃), 3.94-3.97 (m, 1 H, CHOH), 4.13-4.21 (ddd, *J* 14.0, 8.0, 2.0, 1 H, NCH_AH_B), 6.54 (s, 1 H, ArH), 6.65 (s, 1 H, ArH); δ_C (100 MHz, CDCl₃) 26.3 (ArCH₂), 30.1 (CCH₂), 33.7 (CH₂COH), 34.9 (NCH₂), 36.9 (CCH), 37.5 (CH₂COH), 38.4 (NCOCH₂), 55.9 (OCH₃), 56.3 (OCH₃), 62.6 (C), 67.8 (CHOH), 107.6 (ArCH), 112.2 (ArCH), 126.5 (ArC), 133.4 (ArC), 147.4 (ArC), 148.1 (ArC), 176.7 (NC=O); ESIMS *m/z* (%) 318.2 ([M+H]⁺, 100); HRMS (ESI) *m/z* found [M⁺ + H], 318.1700. C₁₈H₂₃NO₄ requires [M+H], 318.1694.

(4a*R*,13b*R*)-11,12-Dimethoxy-1,2,4a,5,8,9-hexahydroindolo[1-*a*]-isoquinoline-3,6-dione (+)-74



A solution of Dess-Martin periodinane solution (0.2 mL, 15 wt % in CH₂Cl₂) was added to the solution of secondary alcohols **73** (30 mg, 0.09 mmol) in CH₂Cl₂ (2 mL) at room temperature. The resulting solution was then stirred for 8 hours. Saturated Na₂S₂O₃ solution (6 mL) was added and the mixture was extracted with CH₂Cl₂ (10 mL). The organic phase was washed with water (6 mL) and brine (6 mL). After drying (MgSO₄), the organic layer was concentrated to yield the crude product, which was further purified by column chromatography (eluent: petroleum ether/AcOEt = 1/2, then 1/4) to give the desired product (+)-**74** (21 mg, 75 %): [α]_D²² +45 (*c* 1.10, CHCl₃); ν_{max} (CHCl₃)/cm⁻¹ 2937, 1716, 1681, 1463, 1362, 1122; δ_H (500 MHz, CDCl₃) 2.10-2.16 (m, 1 H, 5-H_A),

2.24-2.35 (m, 3 H, 1-H, 2-H_A), 2.38-2.43 (m, 1 H, 2-H_B), 2.60-2.76 (m, 3 H, 4-H_A, 5-H_B, 9-H_A), 2.96-3.11 (m, 4 H, 4a-H, 4-H_B, 8-H_A, 9-H_B), 3.86 (s, 3 H, OCH₃), 3.88 (s, 3 H, OCH₃), 4.32-4.40 (m, 1 H, 8-H_B), 6.58 (s, 1 H, ArH), 6.69 (s, 1 H, ArH); δ_{C} (125 MHz, CDCl₃) 27.6 (ArCH₂), 33.6 (CCH₂), 34.8 (CH₂CH₂CO), 35.3 (NCH₂), 37.5 (CCH), 37.8 (NCOCH₂), 43.3 (COCH₂CH), 56.0 (OCH₃), 56.4 (OCH₃), 62.5 (C), 107.2 (ArCH), 111.7 (ArCH), 125.5 (ArC), 134.4 (ArC), 148.3 (ArC), 148.5 (ArC), 172.2 (NC=O), 210.2 (C=O); ESIMS *m/z* (%) 316.2 ([M+H]⁺, 100), 338.1 ([M+Na]⁺, 74); HRMS (ESI) found [M+H]⁺, 316.1554. C₁₈H₂₁NO₄ requires [M+H], 316.1532.

(1S,10bS)-10b-(3-Butenyl)-8,9-dimethoxy-1-(triisopropylsilyloxy)-1,2,3,5,6,10b-hexahydropyrrolo[2,1-a]isoquinoline 75

A solution of AlCl₃ (600 mg, 0.66 mmol) in Et₂O (3 mL) was added dropwise to the solution of LiAlH₄ (2 mL, 1 M in THF) at -15 °C. The resulting solution was then stirred at r.t. for 1 h before was added dropwise into the solution of lactam **60** (209 mg, 0.44 mmol) in THF (2 mL) at -15 °C. The resulting reaction mixture was stirred for 2 h before quenching with 5% NH₃·H₂O (10 mL). The mixture was extracted with EtOAc (200 mL). The organic phase was washed with water (10 mL), brine (10 mL), then dried over anhydrous MgSO₄ and concentrated *in vacuo*. The crude product was purified by flash silica chromatography (eluent: petroleum ether/AcOEt = 4/1 then 2/1) to give the amine **75** (140 mg, 69%) as a colourless oil: $[\alpha]_{\text{D}}^{27} +42$ (*c* 1.78, CHCl₃); ν_{max} . (CHCl₃)/cm⁻¹ 2937, 2866, 1638, 1463, 1358, 1096, 998; δ_{H} (400 MHz, CDCl₃) 0.84-0.93 (m, 21 H, CH(CH₃)₂), 1.52-1.88 (m, 4 H, CH₂CH_AH_BCH=, CH_AH_BCHOSi), 2.08-2.19 (m, 2 H, CH_AH_BCH=, CH_AH_BCHOSi), 2.54-2.72 (m, 2 H, ArCH₂), 2.92-3.26 (m, 4 H, CH₂NCH₂), 3.81 (s, 3 H, OCH₃), 3.83 (s, 3 H, OCH₃), 4.38 (dd, *J* 5.0, 2.5, 1 H, CHOSi), 4.82-4.91(m, 2 H, =CH₂), 5.68-5.77 (m, 1 H,

CH=), 6.54 (s, 1 H, ArH), 6.76 (s, 1 H, ArH); δ_C (100.6 MHz, CDCl₃) 12.8 (SiCH), 17.8 9 (CH₃), 17.9 (CH₃), 27.4 (ArCH₂), 28.4 (CH₂CH=), 33.2 (CH₂COSi), 40.5 (CCH₂), 48.7 (NCH₂), 51.9 (NCH₂), 55.9 (OCH₃), 56.0 (OCH₃), 71.4 (C), 81.2 (CHOSi), 110.5 (ArCH), 111.1 (ArCH), 113.7 (CH₂=), 130.2 (ArC), 130.4 (ArC), 139.6 (CH=), 146.9 (ArC), 147.1 (ArC); ESIMS m/z (%) 460.3 ([M+H]⁺, 100); HRMS (ESI) found [M+H]⁺, 460.3252. C₂₇H₄₆NO₃Si requires [M+H], 460.3241.

(1S,10bS)-10b-(3-Butenyl)-8,9-dimethoxy-1,2,3,5,6,10b-hexahydropyrrolo-[2,1-a]isoquinolin-1-ol 76

A solution of AlCl₃ (600 mg, 4.5 mmol) in Et₂O (6 mL) was added dropwise to the solution of LiAlH₄ (9 mL, 1 M in THF) at -15 °C. The resulting solution was then stirred at r.t. for 1 h before added dropwise into the solution of lactam **60** (1.4 g, 3.0 mmol) in THF (9 mL) at -15 °C. The resulting reaction mixture was then stirred overnight before quenched by addition of 5% NH₃:H₂O (15 mL) carefully. The mixture was then extracted with EtOAc (200 mL). The organic phase was washed with water (10 mL), brine (10 mL), then dried over anhydrous MgSO₄ and concentrated *in vacuo*. The crude product was purified by flash silica chromatography (eluent: petroleum ether/AcOEt = 4/1 then 2/1) to give the alcohol **76** (818 mg, 90%) as a colourless oil. $[\alpha]_D^{27} +37$ (c 1.20, CHCl₃); ν_{\max} . (CHCl₃)/cm⁻¹ 3563, 2937, 2836, 1639, 1609, 1463, 1358, 1096, 998; δ_H (400 MHz, CDCl₃) 1.58-1.64 (m, 2 H, CH_AH_BCH_AH_BCH=), 1.72-1.80 (m, 1 H, CH_AH_BCH₂CH=), 1.91-2.02 (m, 1 H, CH_AH_BCHOH), 2.10-2.23 (m, 2 H, CH_AH_BCH=, CH_AH_BCHOH), 2.60-2.74 (m, 2 H, ArCH₂), 3.00-3.26 (m, 4 H, CH₂NCH₂), 3.87 (s, 3 H, OCH₃), 3.88 (s, 3 H, OCH₃), 4.20 (d, *J* 4.4, 1 H, CHOH), 4.86 (dd, *J* 10.0, 1.6, 1 H, =CH_AH_B), 4.90 (dd, *J* 17.2, 1.6, 1 H, =CH_AH_B), 5.68-5.78 (m, 1 H, CH=), 6.65 (s, 1 H, ArH), 6.68 (s, 1 H, ArH); δ_C (100 MHz, CDCl₃) 27.6

(ArCH₂), 28.7 (CH₂CH=), 31.4 (COHCH₂), 40.9 (CCH₂), 48.9 (NCH₂), 51.9 (CH₂CHO), 55.8 (OCH₃), 56.3 (OCH₃), 71.4 (C), 80.1 (CHOH), 109.1 (ArCH), 111.7 (ArCH), 114.0 (CH₂=), 127.8 (ArC), 131.8 (ArC), 139.2 (CH=), 147.8 (ArC), 147.9 (ArC); ESIMS *m/z* (%) 304.2 ([M+H]⁺, 100); HRMS (ESI) found [M+H]⁺, 304.1898. C₁₈H₂₅NO₃ requires [M+H], 304.1913.

(S)-10b-(3-Butenyl)-8,9-dimethoxy-2,3,5,6-tetrahydropyrrolo[2,1-*a*]isoquinolin- 1-one 77

To a solution of oxalyl chloride (516 mg, 4 mmol) in CH₂Cl₂ (3 mL) at -78 °C was added DMSO (312 mg, 0.6 mmol) dropwise. The resulting solution was then stirred at this temperature for 30 minutes before the alcohol **76** (410 mg, 1.4 mmol) in CH₂Cl₂ (3 mL) was added dropwise. The resulting reaction mixture was then stirred at -78 °C for 2 h. Et₃N (1.9 mL, 14 mmol) was then added. The reaction mixture was warmed to rt before water (10 mL) was then added. The mixture was extracted with CH₂Cl₂ (100 mL). The organic phase was washed with brine (10 mL), dried over anhydrous MgSO₄ and concentrated *in vacuo*. The crude product was purified by flash silica chromatography (eluent: petroleum ether/AcOEt = 2/1) to give the ketone **77** (389 mg, 94%) as a yellow oil. [α]_D²³ -44 (*c* 1.30, CHCl₃); ν_{max} (CHCl₃)/cm⁻¹ 2936, 2850, 1756, 1608, 1463, 1358, 1119, 1104; δ_H (400 MHz, CDCl₃) 1.74-1.90 (m, 2 H, CCH₂), 2.02-2.24 (m, 2 H, CH₂CH=), 2.36-2.42 (m, 3 H, NCH_AH_BCH₂CO), 3.03-3.29 (m, 5 H, ArCH₂, CH₂NCH_AH_B), 3.84 (s, 3 H, OCH₃), 3.87 (s, 3 H, OCH₃), 4.90 (dd, *J* 10.0, 1.6, 1 H, =CH_AH_B), 4.96 (dd, *J* 17.2, 1.6, 1 H, =CH_AH_B), 5.70-5.84 (m, 1 H, CH=), 6.51 (s, 1 H, ArH), 6.95 (s, 1 H, ArH); δ_C (100 MHz, CDCl₃) 21.0 (CH₂), 29.3 (CH₂), 36.4 (CH₂), 38.0 (CH₂), 41.5 (CH₂), 43.6 (CH₂), 55.8 (OCH₃), 55.9 (OCH₃), 68.4 (C), 109.7 (ArCH), 111.6 (ArCH), 114.4 (CH₂=), 125.8 (ArC), 125.9 (ArC), 138.5 (CH=), 147.6 (ArC), 148.0 (ArC), 216.1 (C=O); ESIMS *m/z* (%) 302.2 ([M+H]⁺, 100); HRMS (ESI) found [M+H]⁺, 302.1754. C₁₈H₂₃NO₃ requires [M+H], 302.1756.

(1*S*,10*bR*)-8,9-Dimethoxy-10*b*-(3-oxobutyl)-1-(triisopropylsilyloxy)-1,2,5,6-tetrahydropyrrolo[2,1-*a*]isoquinolin-3-one 78

PdCl₂ (61 mg, 0.34 mmol) and CuCl (171 mg, 1.7 mmol) were dissolved in a mixture of DMF (8 mL) and water (1.5 mL). The reaction mixture was then stirred at r.t. for 2 h before a solution of lactam **61** (818 mg, 1.7 mmol) in DMF (3 mL) was added. The resulting solution was then stirred under an O₂ atmosphere for 20 h. The mixture was extracted with ether (150 mL). The organic phase was then separated and washed with water (10 mL) twice and brine (10 mL). The organic phase was dried over anhydrous MgSO₄ and concentrated *in vacuo*. The crude product was purified by flash silica column (eluent: petroleum ether/AcOEt = 1/1) to give the methyl ketone **78** (731 mg, 86%) as a sticky oil [α]_D²⁶ -79 (*c* 1.60, CHCl₃); ν_{\max} . (CHCl₃)/cm⁻¹ 2936, 2868, 1714, 1682, 1457, 1361, 1113, 1069, 996, 883; δ_{H} (400 MHz, CDCl₃) 1.05-1.10 (m, 21 H, CH(CH₃)₂), 2.00 (s, 3 H, CH₃CO), 2.18-2.24 (m, 3 H, COCH_AH_BCH₂), 2.54-2.78 (m, 5 H, ArCH₂, CH₂CON, COCH_AH_BCH₂), 2.85 (td, *J* 12.8, 4.0, 1 H, NCH_AH_B), 3.75 (s, 3 H, OCH₃), 3.77 (s, 3 H, OCH₃), 4.31 (dd, *J* 12.8, 5.0, 1 H, NCH_AH_B), 4.41 (t, *J* 9.6, 1 H, CHOTIPS), 6.48 (s, 1 H, ArH), 6.80 (s, 1 H, ArH); δ_{C} (100.6 MHz, CDCl₃) 12.4 (SiCH), 17.6 (CH₃), 17.7 (CH₃), 17.8 (CH₃), 17.9 (CH₃), 28.2 (ArCH₂), 29.8 (COCH₃), 30.0 (CCH₂), 34.9 (ArCH₂CH₂), 38.9 (CH₂COMe), 40.6 (NCOCH₂), 55.6 (OCH₃), 55.7 (OCH₃), 66.2 (C), 75.9 (CHOSi), 107.8 (ArCH), 111.4 (ArCH), 124.6 (ArC), 132.2 (ArC), 147.8 (2 x ArC), 169.4 (C=O), 207.1 (C=O); ESIMS *m/z* (%) 490.3 ([M+H]⁺, 93), 512.3 ([M+Na]⁺, 100); HRMS (ESI) found [M+H]⁺, 490.2990. C₂₇H₄₃NO₅Si requires [M+H], 490.2989.

(1*S*,10*bS*)-10*b*-(3-Hydroxybutyl)-8,9-dimethoxy-1,2,3,5,6,10*b*-hexahydro-

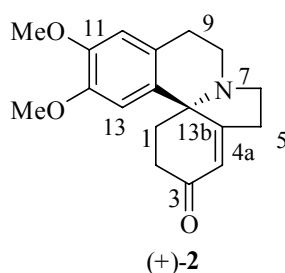
pyrrolo[2,1-*a*]isoquinolin-1-ol **79**

A solution of AlCl₃ (1.5 g, 11 mmol) in Et₂O (10 mL) was added dropwise to the solution of LiAlH₄ (11 mL, 1 M in THF) at -15 °C. The resulting solution was then stirred at r.t. for 1 h before being added dropwise into the solution of lactam **78** (600 mg, 1.2 mmol) in THF (10 mL) at -15 °C. The resulting reaction mixture was then stirred overnight before careful quenching with 5% NH_{3(aq)} solution (5 mL). The mixture was extracted with EtOAc (200 mL) and the organic phase was then washed with water (10 mL), brine (10 mL), dried over anhydrous MgSO₄ and concentrated. The crude product was purified by flash silica column (eluent: petroleum ether/AcOEt = 4/1 then 2/1) to give the diol **79** (189 mg, 48%) as a colourless oil which is a mixture of diastereoisomers with a ratio of 10:9. ν_{\max} (CHCl₃)/cm⁻¹ 3617, 3362, 2936, 2835, 1612, 1463, 1356, 1109, 866; δ_{H} (400 MHz, CDCl₃) 1.06 (d, *J* 6.4, 3 H, CH₃), 1.12 (d, *J* 6.4, 3 H, CH₃), 1.45-1.62 (m, 3 H), 1.78-2.12 (m, 7 H), 2.16-2.30 (m, 2 H), 2.59-2.92 (m, 7 H), 2.97-3.08 (m, 2 H), 3.12-3.30 (m, 2 H), 3.35-3.44 (m, 1 H), 3.67-3.72 (m, 2 H, CHOH), 3.84 (s, 3 H, OCH₃), 3.85 (s, 3 H, OCH₃), 3.87 (s, 3 H, OCH₃), 3.88 (s, 3 H, OCH₃) 4.29-4.36 (m, 2 H, CHOHCH₃), 6.54 (s, 1 H, ArH), 6.57 (s, 1 H, ArH), 6.83 (s, 1 H, ArH), 6.92 (s, 1 H, ArH); δ_{C} (100 MHz, CDCl₃) 23.5 (CH₃), 24.0 (CH₃), 24.3 (CH₂), 27.0 (CH₂), 31.7 (CH₂), 31.8 (CH₂), 32.0 (CH₂), 32.1 (CH₂), 33.9 (CH₂), 34.5 (CH₂), 45.0 (CH₂), 47.7 (CH₂), 47.8 (CH₂), 48.9 (CH₂), 55.8 (OCH₃), 56.2 (OCH₃), 67.4 (CH), 67.8 (C), 68.0 (C), 68.5 (CH), 78.9 (CH), 79.4 (CH), 109.0 (CH), 109.2 (CH), 110.8 (CH), 111.1 (CH), 125.6 (C), 126.8 (C), 131.3 (C), 131.9 (C), 147.46 (C), 147.54 (C), 147.74 (C), 147.76 (C); ESIMS *m/z* (%) 322.20 ([M+H]⁺, 100); HRMS (ESI) found [M+H]⁺, 322.2008. C₁₈H₂₇NO₄ require [M+H]⁺, 322.2018.

(*R*)-8,9-Dimethoxy-10b-(3-oxobutyl)-2,3,5,6-tetrahydropyrrolo[2,1-*a*]isoquinolin-1-one **80**

DMSO (0.11 mL, 1.5 mmol) was added dropwise to the solution of (COCl)₂ (95 mg, 0.75 mmol) in CH₂Cl₂ (2 mL) at -78 °C under nitrogen atmosphere. The resulting solution was then stirred at this temperature for 30 min before a solution of diol **79** (60 mg, 0.19 mmol) in CH₂Cl₂ (2 mL) was added dropwise. The resulting reaction mixture was then stirred at -78 °C for 2 hours, and then Et₃N (0.38 mL, 2.8 mmol) was added dropwise. The reaction mixture was then warmed to room temperature before water (5 mL) was added. The mixture was extracted with CH₂Cl₂ (30 mL). The organic phase was washed with water (5 mL), brine (5 mL), dried over anhydrous MgSO₄ and concentrated *in vacuo*. The crude product was purified by flash silica chromatography (eluent: petroleum ether/AcOEt = 1/2) to give a colorless oil **80** (40 mg, 67%): [α]_D²⁵ +50 (*c* 0.75, CHCl₃); ν_{max} (CHCl₃)/cm⁻¹ 2936, 2850, 1746, 1709; δ_{H} (400 MHz, CDCl₃) 2.11 (s, 3 H, CH₃CO), 2.11-2.26 (m, 3 H, CH₂CH_AH_B), 2.35-2.43 (m, 3 H, CH₂CO, ArCH_AH_B), 2.48-2.54 (m, 1 H, CH₂CH_AH_B), 3.00-3.10 (m, 4 H, ArCH_AH_BCH_AH_BNCH₂), 3.14-3.22 (m, 1 H, ArCH₂CH_AH_BN), 3.82 (s, 3 H, OCH₃), 3.84 (s, 3 H, OCH₃), 6.51 (s, 1 H, ArH), 6.90 (s, 1 H, ArH); δ_{C} (100 MHz, CDCl₃) 21.1 (CH₂), 30.2 (CH₃), 32.6 (CH₂), 36.3 (CH₂), 39.2 (CH₂), 41.3 (CH₂), 43.5 (CH₂), 55.8 (OCH₃), 55.9 (OCH₃), 68.1 (C), 109.6 (ArCH), 111.6 (ArCH), 125.0 (ArC), 126.0 (ArC), 147.6 (ArC), 148.2 (ArC), 208.0 (C=O), 215.9 (C=O); ESIMS *m/z* (%) 318.2 ([M⁺+H], 100), 340.2 ([M+Na]⁺, 18); HRMS found [M+Na]⁺, 340.1519. C₁₈H₂₃NO₄ requires [M+Na], 340.1515.

(S)-11,12-Dimethoxy-1,2,5,6,8,9-hexahydroindolo[1-a]isoquinolin-3-one (+)-2



A solution of diketone **80** (34 mg, 0.107 mmol) and 20% KOH (1.5 mL) in MeOH (30 mL) was heated at 120 °C under a nitrogen atmosphere for 10 hours. The reaction mixture was concentrated and extracted with CH₂Cl₂ (20 mL). The organic phase was washed with water (5 mL), brine (5 mL) and dried over anhydrous MgSO₄. After filtration and concentration, the crude product was purified by flash silica chromatography (eluent: CH₂Cl₂/MeOH = 10/1) to give a yellow oil (+)-**2** (15.9 mg, 50%): [α]_D²⁶ +316 (*c* 0.40, CHCl₃); ν_{max} . (CHCl₃)/cm⁻¹ 2936, 2852, 1666, 1463, 1360, 1107; δ_{H} (400 MHz, CDCl₃) 2.24-2.33 (m, 2 H, 1-H), 2.43-2.68 (m, 4 H, 2-H, 5-H_A, 9-H_A), 2.68-2.92 (m, 2 H, 5-H_B, 6-H_A), 3.03-3.12 (m, 2 H, 9-H_B, 6-H_B), 3.26 (dd, 1 H, *J* 14.4, 7.6, 8-H_A), 3.45-3.52 (m, 1 H, 8-H_B), 3.76 (s, 3 H, OCH₃), 3.88 (s, 3 H, OCH₃), 6.12 (s, 1 H, 4-H), 6.56 (s, 1 H, ArH), 6.66 (s, 1 H, ArH); δ_{C} (100 MHz, CDCl₃) 21.5 (9-CH₂), 28.6 (5-CH₂), 32.8 (2-CH₂), 35.9 (1-CH₂), 40.1 (8-CH₂), 45.7 (6-CH₂), 55.9 (OCH₃), 56.0 (OCH₃), 63.7 (13b-C), 110.2 (ArCH), 112.8 (ArCH), 123.9 (4-CH=), 124.4 (ArC), 125.4 (ArC), 146.9 (ArC), 148.4 (ArC), 168.5 (4a-C), 199.3 (C=O); ESIMS *m/z* (%) 300.2 ([M+H]⁺, 100); HRMS (ESI) found [M+H]⁺, 300.1586. C₁₈H₂₁NO₃ requires [M+H], 300.1594.