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 cm$^3$. $^1$H NMR and $^{13}$C 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 KMnO$_4$, and under UV (254 nm). Enantiomeric excesses were determined by chiral HPLC with a Hewlett-Packard LC1100 using DAICEL chiracel-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.

(1S,5R)-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 Na₂SO₄ and concentrated *in vacuo* to give a colourless solid 28 as a mixture of isomers (680 mg, 95%): \(\nu_{\text{max.}}\) (CHCl₃)/cm\(^{-1}\) 2938, 2838, 1778, 1716, 1391, 1357, 1149, 906; \(\delta_H\) (400 MHz, CDCl₃) 2.97 (t, \(J\) 7.4, 2 H, PhCH₂), 3.47 (d, \(J\) 2.6, 2 H, CHCH), 3.83 (t, \(J\) 7.4, 2 H, NCH₂), 3.87 (s, 3 H, OCH₃), 3.88 (s, 3 H, OCH₃), 4.15 (d, \(J\) 2.6, 2 H, CHClCHCl), 6.68-6.78 (m, 3 H, ArH); \(\delta_C\) (100.6 MHz, CDCl₃): 32.2 (ArCH₂), 39.4 (NCH₂), 47.5 (CH), 56.0 (OCH₃), 56.1 (OCH₃), 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 [M\(^+\)], 357.0535. C₁₆H₁₇NO₄Cl₂ requires M, 357.0536.
(1S,5R)-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; νmax. (CHCl3)/cm⁻¹ 2938, 1703, 1392, 1154, 908; δH (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); δC (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.

(1S,5R)-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: [α]D₂₅ +131 (c 4.50, CHCl₃); νmax. (CHCl₃)/cm⁻¹ 2938, 2838, 1755, 1682, 1593, 1387, 1357, 986; δH (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); δC (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% iPrOH 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.

(1R,5S)-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 °C. The resulting solution was then warmed to rt slowly until the reaction was completed. The reaction was quenched with saturated aqueous NaHCO₃ 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<sub>max</sub> (CHCl₃)/cm⁻¹ 3584, 2937, 1673, 1492, 1028; δ<sub>H</sub> (400 MHz, d-acetone) 1.48-1.56 (m, 1 H, CH₆H₂COH), 1.92-2.04 (m, 1 H, CH₆H₂COH), 2.20-2.48 (m, 2 H, CH₂C=), 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, CH=), 5.85-6.02 (m, 1 H, CH=CH₂), 6.74 (d, J 2.0, 1 H, CH=CH), 6.76 (d, J 2.0, 1 H, CH=CH₂), 6.80-6.87 (m, 3 H, ArH); δ<sub>C</sub> (100 MHz, d-acetone) 30.0 (CH₂), 35.9 (CH₂), 35.9 (CH₂), 42.0 (CH₂), 49.2 (CH), 51.4 (CH), 56.1 (OCH₃), 56.2 (OCH₃), 89.8 (COH), 113.0 (ArCH), 113.8 (ArCH), 114.8 (CH₂=), 121.6 (ArCH), 133.3 (ArC), 139.3 (CH=), 140.6 (CH=), 142.1 (CH=), 149.0 (ArC), 150.0 (ArC), 174.3 (NC=O); ESIMS m/z (%) 366.2 ([M+Na]⁺, 100), 326.2 ([M-H₂O]⁺, 97); HRMS (ESI) found M⁺, 343.1784. C₂₀H₂₅NO₄ requires M⁺, 343.1784.


TMSOTf (6 mL, 33 mmol) was added in one portion to the solution of hydroxyl lactam 23 (5.7 g, 16.5 mmol) in CH₂Cl₂ (50 mL) at −78 °C. The resulting reaction mixture was left in a cold room (−4 °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: νₘₐₓ. (CHCl₃)/cm⁻¹ 2938, 2856, 1667, 1360, 1124, 904; δH (400 MHz, CDCl₃) 1.90-1.92 (m, 1 H, CCH₆H₆), 2.04-2.07 (m, 1 H, CCH₆H₆), 2.15-2.18 (m, 2 H, CH₂CH=), 2.64 (ddd, J 16.4, 5.0, 1.2, 1 H, ArCH₆CH₆), 3.05-3.10 (ddd, J 16.4, 12.0, 7.2, 1 H, ArCH₆CH₆), 3.11-3.21 (ddd, J 14.0, 12.0, 5.0, 1 H, NCH₆CH₆), 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, NCH₆CH₆), 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); δC (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.

(4aS,5R,13bS)-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 ballon) 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%): ν_{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_{A}H_{B}), 2.94-3.02 (m, 1 H, ArCH_{A}H_{B}), 3.10 (d, J 8.0, 1 H, CHCH=CH), 3.29-3.36 (m, 2 H, CHCO, NCH_{A}H_{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_{A}H_{B}), 5.26-5.32 (m, 2 H, CH=CH_2), 5.73-5.86 (m, 2 H, CH=CH_2, CH=CHCH), 6.05-6.12 (m, 1 H, CH=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 (CH_2=), 125.2 (ArC), 126.5 (CH=), 128.8 (CH=), 133.5 (ArC), 133.8 (CH=), 147.6 (ArC), 148.0 (ArC), 172.8 (NC=O); ESIMS m/z (%) 326.2 ([M+H]^+, 100); HRMS (ESI) found M^+, 325.1670. C_{20}H_{23}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%): ν_{max.} (CHCl_3)/cm^{-1} 3582, 2960, 2927, 1723, 1688, 1463, 1382, 1264,
1101, 1050, 874; $\delta_H$ (400 MHz, CDCl$_3$) 1.55-1.65 (m, 1 H, CCH$_2$CH$_A$H$_B$), 1.82-1.93 (m, 2 H, CCH$_A$H$_B$CH$_A$H$_B$), 2.16-2.23 (m, 1H, CCH$_A$H$_B$CH$_2$), 2.52 (dd, J 16.5, 5.1, 1 H, ArCH$_A$CH$_B$), 2.85 (t, J 7.6, 1 H, CHCHOH), 3.07-3.18 (m, 2 H, ArCH$_A$CH$_B$, CHCH=), 3.19-3.28 (m, 1 H, NCH$_A$CH$_B$), 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$_A$H$_B$), 5.41 (dd, 1 H, J 19.0, 1.2, 1 H, CH$_A$H$_B$=), 5.46 (dd, J 10.4, 1.2, 1 H, CH$_A$H$_B$=), 6.00 (ddd, J 19.0, 10.4, 8.6, 1 H, CH=CH$_2$), 6.51 (s, 1 H, ArH), 6.86 (s, 1 H, ArH); $\delta_C$ (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 (CH$_2$=), 126.1 (ArC), 132.4 (CH=), 132.5 (ArC), 147.6 (ArC), 148.2 (ArC), 177.9 (NC=O); ESIMS m/z (%) 360.2 ([M+H]$^+$, 66), 382.2 ([M+Na]$^+$, 66); HRMS (ESI) found M$^+$, 359.1733. C$_{20}$H$_{25}$NO$_5$ requires M, 359.1725.

**(4aR,13bS)-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; $\nu_{\text{max.}}$ (CHCl$_3$)/cm$^{-1}$ 3552, 2936, 2836, 1683, 1454, 1363, 908; $\delta_H$ (500 MHz, CDCl$_3$) 2.02-2.26 (m, 4 H, CCH$_2$CH$_2$), 2.87-3.01 (m, 3 H, CH, ArCH$_2$), 3.42-3.48 (m, 1 H, NCH$_A$H$_B$), 3.77 (s, 3 H, OCH$_3$), 3.85 (s, 3 H, OCH$_3$), 4.15-4.22 (m, 1 H, NCH$_A$H$_B$), 5.39 (dd, J 10.5, 1.0, 1 H, CH=CH$_A$H$_B$), 5.50 (dd, J 17.5, 1.0,
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, CCH₂H₂HB), 2.21-2.19 (m, 1 H, CCH₂CH₀HB), 2.32-2.36 (m, 1 H, CCH₂H₂HB), 2.41-2.47 (m, 1 H, CCH₂H₂CH₂), 2.99 (td, J 11.2, 2.0, 2 H, ArCH₂), 3.56 (dt, J 10.4, 5.6, 1 H, NCH₃H₃B), 3.78 (s, 3 H, OCH₃), 3.86 (s, 3 H, OCH₃), 4.11 (td, J 10.4, 5.6, 1 H, NCH₃H₃B), 5.46 (dd, J 9.0, 2.0, 1 H, CH=CH₂HB), 6.30-6.34 (m, 1 H, CH=CH), 6.46 (dd, J 14.0, 9.0, 1 H, CH=CH₂HB), 6.59 (dd, J 14.0, 9.0, 1 H, CH=CH₂HB), 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.

(4αS,5R,13bS)-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 \textit{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; \(\nu_{\text{max.}}\) (CHCl\(_3\))/cm\(^{-1}\) 2935, 2854, 1668, 1463, 1362, 1115, 872; \(\delta_{\text{H}}\) (400 MHz, CDCl\(_3\)) 1.71 (s, 3 H, CH\(_3\)), 1.77 (s, 3 H, CH\(_3\)), 1.75-2.24 (m, 4 H, CH\(_2\)CH\(_2\)), 2.68-2.77 (m, 1 H, ArCH\(_A\)H\(_B\)), 2.95-3.14 (m, 2 H, CHCH=CH, ArCH\(_A\)H\(_B\)), 3.26-3.34 (m, 1 H, NCH\(_A\)H\(_B\)), 3.51 (t, \(J\ 9.6, 1\ H, \ CHCH=CH\)), 3.83 (s, 3 H, OCH\(_3\)), 3.86 (s, 3 H, OCH\(_3\)), 4.17-4.24 (m, 1 H, NCH\(_A\)H\(_B\)), 5.15 (d, \(J\ 9.6, 1\ H, CH=CH\)), 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); \(\delta_{\text{C}}\) (100 MHz, CDCl\(_3\)) 18.6 (CH\(_3\)), 22.1 (CH\(_2\)), 26.0 (CH\(_3\)), 27.1 (CH\(_2\)), 33.7 (CH\(_2\)), 35.1 (CH\(_2\)), 43.4 (CH), 45.6 (CH), 55.9 (OCH\(_3\)), 56.1 (OCH\(_3\)), 61.1 (C), 108.2 (ArCH), 111.9 (ArCH), 119.8 (CH=CH), 125.4 (C), 126.9 (CH=CH), 128.2 (CH=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. C\(_{22}\)H\(_{27}\)NO\(_3\) requires \(M\), 353.1998. Minor product 38: colourless oil; more polar; \(\nu_{\text{max.}}\) (CHCl\(_3\))/cm\(^{-1}\) 2935, 2854, 1674, 1463, 1362, 1120, 1044, 906, 868; \(\delta_{\text{H}}\) (400 MHz, CDCl\(_3\)) 1.63 (s, 3 H, CH\(_3\)), 1.71 (s, 3 H, CH\(_3\)), 1.88-2.29 (m, 5 H, CH\(_A\)H\(_B\)CH=CH, CCH\(_2\)CH\(_2\)), 2.41-2.70 (m, 3 H, ArCH\(_A\)H\(_B\), CHCO, CH\(_A\)H\(_B\)CH=CH), 2.97-3.14 (m, 2 H, CHCH=CH, ArCH\(_A\)H\(_B\)), 3.20-3.30 (m, 1 H, NCH\(_A\)H\(_B\)), 3.83 (s, 3 H, OCH\(_3\)), 3.86 (s, 3 H, OCH\(_3\)), 4.20-4.25 (m, 1 H, NCH\(_A\)H\(_B\)), 5.20 (t, \(J\ 6.1, 1\ H, CH=CH\)), 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); \(\delta_{\text{C}}\) (100 MHz, CDCl\(_3\)) 18.2 (CH\(_3\)), 21.8 (CH\(_2\)), 25.9 (CH\(_3\)), 26.8 (CH\(_2\)), 26.9 (CH\(_2\)), 33.7 (CH\(_2\)), 35.1 (CH\(_2\)), 42.1 (CH), 46.3 (CH), 55.9 (OCH\(_3\)), 56.2 (OCH\(_3\)), 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.

(4aS,5R,13bS,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_{2}Cl_{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: \nu_{\text{max}}. (CHCl_{3})/cm^{-1} 2936, 2846, 1672, 1362, 1106; \delta_{\text{H}} (500
MHz, CDCl_{3}) 1.82-1.89 (m, 1 H, CCH_{2}CH_{2}A), 2.03-2.12 (m, 2 H, CCH_{2}H_{2}CH_{2}H_{2}), 2.19-2.27
(m, 1 H, CCH_{2}H_{2}CH_{2}), 2.75-2.82 (m, 1 H, ArCH_{2}H_{2}), 2.98-3.08 (m, 1 H, ArCH_{2}H_{2}), 3.15-3.20
(m, 1 H, NCH_{2}H_{2}), 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_{2}H_{2}), 5.90 (dt, J 10.2, 2.0, 1 H, CH_{2}CH=CH)
6.07-6.12 (m, 1 H, CH_{2}CH=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); \delta_{\text{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^{+},

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

The suspension of PdCl$_2$ (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 MgSO$_4$ 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%): $\nu_{\text{max.}}$ (CHCl$_3$)/cm$^{-1}$ 2935, 2835, 1723, 1694, 1456, 1392, 1361, 1120, 870; $\delta_H$ (500 MHz, CDCl$_3$) 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, OCH$_3$), 3.81 (s, 3 H, OCH$_3$), 4.10-4.19 (m, 1 H, NCH$_2$H$_3$), 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); $\delta_C$ (125 MHz, CDCl$_3$) 21.7 (CH$_2$), 26.8 (CH$_2$), 33.8 (CH$_2$), 35.0 (CH$_2$), 39.9 (CH), 41.4 (CH), 42.6 (CH$_2$), 55.8 (OCH$_3$), 56.0 (OCH$_3$), 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. $\text{C}_{26}\text{H}_{23}\text{NO}_4$ requires $M$, 341.1626.

(4a$S$,5$S$,13b$S$,E)-5-(2-(tert-Butyldimethylsilyloxy)vinyl)-11,12-dimethoxy-
TBSOTf (0.32 mL, 1.4 mmol) was added dropwise to the solution of aldehyde 41 (240 mg, 0.7 mmol) in CH$_2$Cl$_2$-Et$_3$N (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 CH$_2$Cl$_2$ (50 mL). The organic phase was washed with water (10 mL), brine (10 mL), then 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 the product as a pale yellow foam 42 (100 mg, 31%), 42 mg starting material aldehyde 41 was recovered. Colourless oil; more polar; $\nu_{\text{max}}$ (CHCl$_3$)/cm$^{-1}$ 2931, 2856, 1668, 1463, 1362, 1128, 870; $\delta_{\text{H}}$ (400 MHz, CDCl$_3$) 0.13 (s, 6 H, CH$_3$), 0.89 (s, 9 H, CH$_3$), 1.73-1.80 (m, 1 H, CCH$_AH_B$CH$_2$), 1.97-2.05 (m, 2 H, CCH$_AH_B$CH$_A$H$_B$), 2.13-2.19 (m, 1 H, CCH$_2$CH$_A$H$_B$), 2.69-2.75 (m, 1 H, ArCH$_AH_B$), 2.94-3.03 (m, 2 H, CHCHCO, ArCH$_A$H$_B$), 3.12 (t, 1 H, J 9.6, CHCHCO), 3.29 (ddd, 1 H, J 13.2, 10.4, 5.6, NCH$_A$CH$_B$), 3.81 (s, 3 H, OCH$_3$), 3.84 (s, 3 H, OCH$_3$), 4.15 (m, 1 H, J 13.2, 7.2, 3.2, NCH$_A$CH$_B$), 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); $\delta_{\text{C}}$ (100 MHz, CDCl$_3$) $-$5.2 (SiCH$_3$), 18.3 (C), 22.1 (CH$_2$), 25.7 (CH$_3$), 27.0 (CH$_2$), 33.4 (CH$_2$), 35.1 (CH$_2$), 43.5 (CH), 45.6 (CH), 55.9 (OCH$_3$), 56.0 (OCH$_3$), 60.9 (C), 106.7 (CH=CHOSi), 108.2 (ArCH), 111.8 (ArCH), 125.3 (C), 126.9 (CH=), 128.4 (CH=), 133.6 (C), 143.8 (CH=CHOSi), 147.5 (C), 147.9 (C), 174.1 (NC=O); ESIMS m/z (%) 456.3 ([M+H]$^+$, 100), 478.2 ([M+Na]$^+$, 10); HRMS (ESI) found [M+H]$^+$, 456.2583. C$_{26}$H$_{37}$NO$_4$Si requires [M+H]$^+$, 456.2565.

(3R,4R,4aS,5R,13bS)-3,4-Dibromo-11,12-dimethoxy-5-vinyl-1,2,3,4,4a,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; νmax. (CHCl₃)/cm⁻¹ 2958, 2854, 1696, 1463, 1359, 1123, 907; δH (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, ArCH₃H₂B), 3.06 (dd, J 9.0, 7.0, 1 H, CHCON), 3.13-3.18 (m, 2 H, NCH₃H₂B, ArCH₃H₂B), 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, NCH₃H₂B), 5.30 (d, J 17.0, 1.5, 1 H, CH₃H₂=CH), 5.41 (dd, J 10.0, 1.5, 1 H, CH₃H₂=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); δC (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.

(4aS,5S,13bS)-5-(Hydroxymethyl)-11,12-dimethoxy-1,2,4a,5,8,9-hexahydroindo-lo[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, CCHₐHₗₜCH₂), 2.01-2.06 (m, 2 H, CCHₐHₗₜCH₂Hₗₜ), 
2.19-2.23 (m, 1 H, CCH₂CHₐHₗₜ), 2.57-2.63 (m, 2 H, CHCH₁CO, ArCH₁Hₗₜ), 2.84-2.92 (m, 2 H, 
CHCH₁CO, ArCH₁Hₗₜ), 3.37-3.43 (m, 1 H, NCH₁Hₗₜ), 3.76-3.80 (m, 1 H, CHₐHₗₜOH), 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, NCH₁CHₗₜHₗₜ, CH₁HₗₜOH), 
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. C_{19}H_{23}NO₄ 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; [α]D²⁵ =−204 (c 0.95, CHCl₃); νmax. (CHCl₃)/cm⁻¹ 3612, 3506, 2938, 2838, 1710, 1682, 1455, 1362, 1142; δH (400 MHz, d-acetone) 1.63-1.75 (m, 1 H, CCH₂HB), 1.85-2.00 (m, 1 H, CCH₂HB), 2.02-2.20 (m, 2 H, CH₂CH=), 2.25 (dd, J 17.2, 3.2, 1 H, NCOCH₂HB), 2.62 (dd, J 17.2, 6.8, 1 H, NCOCH₂HB), 2.75-2.95 (m, 2 H, ArCH₂), 3.25 (m, 1 H, NCH₂HB), 3.50 (m, 1 H, NCH₂HB), 3.76 (s, 3 H, OCH₃), 3.80 (s, 3 H, OCH₃), 4.30 (dd, J 6.8, 3.2, 1 H, CH₂OH), 4.56 (s, 1 H, OH), 4.93 (s, 1 H, OH), 4.94 (dd, J 10.0, 2.0, 1 H, CH₂HB), 5.04 (dd, J 17.2, 2.0, 1 H, CH₂HB), 5.83-5.90 (m, 1 H, CH=CH₂), 6.60-6.80 (m, 3H, ArH); δC (100.6 MHz, d-acetone) 28.8 (CH₂CH=), 35.7 (ArCH₂), 36.7 (COCH₂), 39.5 (NCOCH₂), 41.8 (NCH₂), 56.1 (OCH₃), 56.2 (OCH₃), 69.1 (CH₂OH), 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-hexahydropyrro-
lo[2,1-a]isoquinolin-1-yl acetate 57

Acetic anhydride (229 mg, 2.2 mmol), triethylamine (252 mg, 2.5 mmol) and 4-N,N-dimethylaminopyridine (12 mg, 0.1 mmol) were added to a solution of alcohol 56 (335 mg, 1 mmol) in CH$_2$Cl$_2$ (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 CH$_2$Cl$_2$ (100 mL). The organic phase was washed with water (10 mL), brine (10 mL), then dried over MgSO$_4$ and concentrated in vacuo. The crude product was dissolved in CH$_2$Cl$_2$ (10 mL) and BF$_3$OEt$_2$ (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 CH$_2$Cl$_2$ (50 mL), the organic phase was washed with saturated aqueous NaHCO$_3$ solution (10 mL), water (10 mL) and brine (10 mL), then dried over MgSO$_4$ 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]$_D$$^{25}$ = −243 (c 2.50, CHCl$_3$); $\nu_{\text{max}}$ (CHCl$_3$)/cm$^{-1}$ 2937, 2253, 1744, 1687, 1463, 898; δ$_H$ (400 MHz, CDCl$_3$) 1.90-2.10 (m, 4 H, 2CH$_2$), 2.20 (s, 3 H, COCH$_3$), 2.50-2.60 (ddd, $J$ 17.0, 8.7, 1.2, 1 H, CH$_{\text{A}}$H$_{\text{B}}$CON), 2.60-2.70 (dd, $J$ 17.0, 3.7, 1 H, ArCH$_{\text{A}}$H$_{\text{B}}$), 2.82-2.90 (m, 1 H, ArCH$_{\text{A}}$H$_{\text{B}}$), 2.92 (dd, $J$ 17.0, 9.0, 1 H, CH$_{\text{A}}$H$_{\text{B}}$CON), 3.01-3.12 (m, 1H, NCH$_{\text{A}}$H$_{\text{B}}$), 3.83 (s, 3 H, OCH$_3$), 3.88 (s, 3 H, OCH$_3$), 4.42 (ddd, $J$ 13.0, 6.5, 1.2, 1 H, NCH$_{\text{A}}$H$_{\text{B}}$), 5.00 (m , 2 H, CH$_2$=CH), 5.30 (dd, $J$ 9.0, 3.7, 1 H, CHOAc), 5.70-5.80 (m, 1 H, CH=CH$_2$), 6.57 (s, 1 H, ArH), 6.68 (s, 1 H, ArH); δ$_C$ (100.6 MHz, CDCl$_3$) 21.2 (CH$_3$), 27.9 (CH$_2$), 29.1 (CH$_2$), 35.2 (CH$_2$), 36.6 (NCOCH$_2$), 37.8 (NCH$_3$), 55.9 (OCH$_3$), 56.0 (OCH$_3$), 65.2 (C), 75.7 (CH), 107.5 (ArCH), 111.6 (ArCH), 115.2 (CH$_2$=), 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$_3$); $\nu$ max. (CHCl$_3$)/cm$^{-1}$ 2937, 2847, 2936, 1681, 1360, 1108; $\delta$$_H$ (400 MHz, CDCl$_3$) 1.86-1.95 (m, 2 H, CCH$_2$), 2.01-2.10 (m, 2 H, CH$_2$CH=), 2.67 (dd, $J$ 16.1, 4.0, 1 H, ArCH$_A$H$_B$), 2.94 (ddd, $J$ 16.1, 12.0, 6.6, 1 H, ArCH$_A$H$_B$), 3.18 (ddd, 1 H, J 13.3, 12.0, 4.0, NCH$_A$H$_B$), 3.83 (s, 3 H, OCH$_3$), 3.88 (s, 3 H, OCH$_3$), 4.40 (dd, $J$ 13.3, 6.6, 1 H, NCH$_A$H$_B$), 5.00 (m, 2 H, CH$_2$=), 5.70-5.80 (m, 1 H, $CH$=CH$_2$), 6.18 (d, $J$ 5.8 Hz, 1H, CH=), 6.60 (s, 1 H, ArH), 6.70 (s, 1 H, ArH), 7.29 (d, $J$ 5.8, 1 H, CH=); $\delta$$_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% iPrOH 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 CH$_2$Cl$_2$ (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 CH$_2$Cl$_2$ (100 mL). The organic phase was washed with saturated aqueous NaHCO$_3$ (10 mL), H$_2$O (10 mL) and brine (10 mL). The organic phase was dried over MgSO$_4$ 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; [α]$_D$ $^{31}$ +12 (c 2.37, CHCl$_3$); $\nu_{\text{max.}}$ (CHCl$_3$)/cm$^{-1}$ 3487, 2943, 2866, 1682, 1463, 1352, 1096, 883; $\delta_H$ (400 MHz, d-acetone) 1.03-1.24 (m, 21 H, SiCH(CH$_3$)$_2$), 1.70-1.91 (m, 2 H, CH$_2$COH), 1.94-2.21 (m, 2 H, CH$_2$CH=), 2.30 (dd, J 16.8, 2.4, 1 H, CH$_A$H$_B$CO), 2.75 (dd, J 16.8, 6.0, 1 H, CH$_A$H$_B$CO), 2.80-2.91 (m, 2 H, ArCH$_2$), 3.18-3.29 (m, 1 H, NCH$_A$H$_B$), 3.48-3.53 (m, 1 H, NCH$_A$H$_B$), 3.79 (s, 3 H, OCH$_3$), 3.82 (s, 3 H, OCH$_3$), 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$_A$H$_B$=CH), 5.04 (dd, 1 H, J 17.2, 2.0, CH$_A$H$_B$=CH), 5.78-5.88 (m, 1 H, CH$_2$=CH), 6.76-7.01 (m, 3 H, ArH); $\delta_C$ (100 MHz, CDCl$_3$) 13.0 (CHSi), 18.4 (CH$_3$), 24.5 (CH$_2$COH), 35.9 (ArCH$_2$), 36.3 (CH$_2$CH=), 40.6 (CH$_2$CO), 41.7 (NCH$_2$), 56.1 (OCH$_3$), 71.2 (CHOSi), 95.0 (COH), 112.9 (ArCH), 113.7 (ArCH), 115.2 (CH$_2$=), 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-H$_2$O]$^+$, 57), 492.3 ([M+H]$^+$, 100), 514.3 ([M+Na]$^+$, 48); HRMS (ESI) found [M+H]$^+$, 492.3140. C$_{27}$H$_{45}$NO$_5$Si requires [M+H]$^+$, 492.3150. Minor diastereoisomer: colourless oil; more polar; $\delta_H$ (400 MHz, d-acetone) 1.03-1.24 (m, 21 H, SiCH(CH$_3$)$_2$), 1.72-2.04
(m, 3 H, C\textsubscript{6}H\textsubscript{5}CH\textsubscript{2}H\textsubscript{B}), 2.23-2.39 (m, 2 H, C\textsubscript{6}H\textsubscript{5}CH\textsubscript{2}H\textsubscript{B}, C\textsubscript{6}H\textsubscript{5}CH\textsubscript{2}CON), 2.74 (dd, J 16.7, 8.0, 1 H, C\textsubscript{6}H\textsubscript{5}CH\textsubscript{2}CON), 2.79-2.86 (m, 1 H, ArCH\textsubscript{2}H\textsubscript{B}), 2.96 (ddd, J 13.2, 9.1, 7.5, 1 H, ArCH\textsubscript{2}H\textsubscript{B}), 3.20 (ddd, J 13.5, 9.1, 7.5, 1 H, NCH\textsubscript{2}H\textsubscript{B}), 3.65 (ddd, J 13.5, 9.3, 4.7, 1 H, NCH\textsubscript{2}H\textsubscript{B}), 3.83 (s, 3 H, OCH\textsubscript{3}), 3.86 (s, 3 H, OCH\textsubscript{3}), 4.22 (t, 1 H, J 8.0, CHOSi), 4.95 (dd, 1 H, J 6.0, 2.0, CH\textsubscript{2}H\textsubscript{B}=CH), 4.99 (dd, 1 H, J 17.2, 2.0, CH\textsubscript{2}H\textsubscript{B}=CH), 5.70-5.80 (m, 1 H, CH\textsubscript{2}=CH\textsubscript{F}), 6.72-6.80 (m, 3 H, ArH); δ\textsubscript{C} (100 MHz, CDCl\textsubscript{3}) 12.2 (CHSi), 17.9 (CH\textsubscript{3}), 27.8 (CH\textsubscript{2}COH), 33.9 (ArCH\textsubscript{2}), 34.4 (CH\textsubscript{2}CH=), 40.1 (CH\textsubscript{2}CO), 41.4 (NCH\textsubscript{2}), 55.9 (OCH\textsubscript{3}), 77.1 (CHOSi), 94.4 (COH), 111.3 (ArCH), 112.2 (ArCH), 115.0 (CH\textsubscript{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\textsubscript{27}H\textsubscript{45}NO\textsubscript{5}Si requires [M+H]+, 492.3145.

(1S,10bS)-10b-(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\textsubscript{2}Cl\textsubscript{2} (30 mL) was treated with BF\textsubscript{3}.Et\textsubscript{2}O (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\textsubscript{2}Cl\textsubscript{2} (100 mL). The organic phase was washed with water (10 mL) and brine (10 mL). The organic phase was dried over MgSO\textsubscript{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; [α]\textsubscript{D}\textsuperscript{25} +133 (c 0.80, CHCl\textsubscript{3}); ν\textsubscript{max.} (CHCl\textsubscript{3})/cm\textsuperscript{-1} 2943, 2866, 1678, 1463, 1102, 883; δ\textsubscript{H} (500 MHz, CDCl\textsubscript{3}) 0.81-0.87 (m, 21 H, 3CH(CH\textsubscript{3})\textsubscript{2}), 1.85-2.05 (m, 4 H, CH\textsubscript{2}CH\textsubscript{2}), 2.37 (d, J 17.0, 1 H, ArCH\textsubscript{2}H\textsubscript{B}), 2.60 (dd, J 15.0, 3.0,
1 H, CH₃H₂CON), 2.72-2.78 (m, 1 H, ArCHA₂H), 2.95-3.04 (m, 2 H, NCH₂H₂B, CH₂H₂BCON), 3.84 (s, 3 H, OCH₃), 3.85 (s, 3 H, OCH₃), 4.45-4.49 (m, 2 H, NCH₂H₂B, CHOTIPS), 4.93 (m, 2 H, C₂H₂=CH), 5.64-5.71 (m, 1 H, CH=CH₂), 6.58 (s, 1 H, ArH), 6.64 (s, 1 H, ArH); δC (125 MHz, CDCl₃) 12.7 (CH), 17.8 (CH₂), 17.9 (CH₃), 29.1 (CH₂), 29.4 (CH₂), 37.6 (CH₂), 39.6 (CH₂), 41.9 (NCH₂), 56.0 (OCH₃), 70.7 (C), 76.3 (CH), 109.0 (ArCH), 111.8 (ArCH), 115.2 (CH₂=), 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. C₂₇H₄₃NO₄Si requires [M+H]⁺, 474.3064. Minor product 61: colourless oil; more polar; [α]D²³ − 161 (c 0.70, CHCl₃); νmax. (CHCl₃)/cm⁻¹ 2945, 2868, 1678, 1462, 1110, 883; δH (400 MHz, CDCl₃) 1.08-1.16 (m, 21 H, CH(CH₃)₂), 1.93-2.03 (m, 2 H, CH₂), 2.16-2.32 (m, 2 H, CH₂), 2.62-2.72 (m, 3 H, ArCH₂, CH₃H₂CON), 2.80-2.89 (m, 1 H, CH₃H₂CON), 2.98 (td, J 12.4, 4.0, 1 H, CH₃H₂BN), 3.86 (s, 6 H, OCH₃), 4.42-4.50 (m, 2 H, CH₃H₂BN, CHOTIPS), 4.92-5.00 (m, 2 H, CH₂=CH), 5.71-5.78 (m, 1 H, CH=), 6.56 (s, 1 H, ArH), 6.93 (s, 1 H, ArH); δC (100 MHz, CDCl₃) 12.7 (SiCH), 18.2 (CH₃), 28.6 (CH₂), 29.3 (CH₂), 35.2 (CH₂), 36.0 (CH₂), 40.8 (NCH₂), 55.9 (OCH₃), 56.0 (OCH₃), 76.3 (CHOSi), 108.1 (ArCH), 111.6 (ArCH), 114.8 (CH₂=), 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. C₂₇H₄₃NO₄Si 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: [α]D25 +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
erther/AcOEt = 1/1) to give the acetate corresponding to 60 (130 mg, 78%) as a colourless oil: [α]D25
+112 (c 0.85, CHCl3); v max. (CHCl3)/cm−1 2938, 2836, 1738, 1682, 1463, 1363, 1042, 907; δH (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,
CHAHBPh), 2.65 (dd, J 15.6, 3.2, 1 H, CHAHBCON), 2.80-2.88 (m, 1 H, CHAHBPh), 3.00-3.11 (m, 2
H, CHAHBCON, CHAHBN), 3.83 (s, 3 H, OCH3), 3.87 (s, 3 H, OCH3), 4.44 (dd, J 13.2, 5.6, 1 H,
CHAHBn), 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); δC (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-tetrahydropyrrololo[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); νmax. (CHCl₃)/cm⁻¹ 2937, 2836, 1738, 1683, 1613, 1456, 1363, 1114, 1041, 998; δH (400 MHz, CDCl₃) 2.12 (s, 3 H, CH₃), 2.52-2.61 (m, 2 H, ArCHA_HB, CHA_HBCON), 2.85-2.95 (m, 2 H, ArCHA_HB,
$^{1}$H and $^{13}$C NMR spectra: $\delta$H (400 MHz, CDCl$_3$) 1.06-1.13 (m, 21 H, SiCH(CH$_3$)$_2$), 2.57 (dd, $J$ 18.0, 5.0, 1 H, CH$_A$H$_B$CON), 2.85 (t, $J$ 8.0, 2 H, ArCH$_2$), 2.98 (dd, $J$ 18.0, 8.0, 1 H, CH$_A$H$_B$CON), 3.72 (dd, $J$ 9.0, 6.5, 1 H, CH$_A$H$_B$N), 3.85 (s, 3 H, OCH$_3$), 3.87 (s, 3 H, OCH$_3$), 4.63 (dd, $J$ 8.0, 5.0, 1 H, CHOSi), 6.73-6.79 (m, 3 H, ArH), 6.98 (s, 1 H, ArH); $\delta$C (100 MHz, CDCl$_3$) 12.1 (CH$_3$), 27.5 (ArCH$_2$), 37.4 (NCH$_2$), 37.8 (COCH$_2$), 55.9 (OCH$_3$), 62.8 (NCH), 73.8 (CHOAc), 107.9 (ArCH), 111.7 (ArCH), 125.6 (ArCH$_2$), 126.1 (ArC), 148.4 (ArC), 170.5 (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. C$_{16}$H$_{19}$NO$_5$ 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 $^\circ$C for 5 h and concentrated in vacuo. The mixture was then extracted with CH$_2$Cl$_2$ (100 mL). The organic phase was washed with saturated aqueous NaHCO$_3$ (10 mL), followed by water (10 mL) then brine (10 mL), dried (MgSO$_4$), 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 CH$_2$Cl$_2$ (10 mL) at 0 $^\circ$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 CH$_2$Cl$_2$ (50 mL). The organic phase was washed with 1 M HCl (10 mL), followed by water (10 mL) then brine (10 mL), dried (MgSO$_4$) and concentrated in vacuo to give a pure yellow oil 64 which was used for the next step without further purification: $[\alpha]_D^{21}$ = -32 (c 2.80, CHCl$_3$); $\nu$ max. (CHCl$_3$)/cm$^{-1}$ 2944, 2868, 2839, 1592, 1463, 1351, 1140, 883; $\delta$H (400 MHz, CDCl$_3$) 1.06-1.13 (m, 21 H, SiCH(CH$_3$)$_2$), 2.57 (dd, $J$ 18.0, 5.0, 1 H, CH$_A$H$_B$CON), 2.85 (t, $J$ 8.0, 2 H, ArCH$_2$), 2.98 (dd, $J$ 18.0, 8.0, 1 H, CH$_A$H$_B$CON), 3.72 (dd, $J$ 9.0, 6.5, 1 H, CH$_A$H$_B$N), 3.85 (s, 3 H, OCH$_3$), 3.87 (s, 3 H, OCH$_3$), 4.63 (dd, $J$ 8.0, 5.0, 1 H, CHOSi), 6.73-6.79 (m, 3 H,
ArH); δC (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; [α]D 20 −87 (c 2.80, CHCl3); νmax. (CHCl3)/cm−1 2943, 2867, 1683, 1613, 1461, 1363, 1132, 1089, 996, 883; δH (400 MHz, CDCl3) 1.04-1.16 (m, 21 H, SiCH(CH3)2), 2.59-2.94 (m, 5 H, NCH2Hb, ArCH2, CH2CON), 3.85 (s, 3 H, OCH3), 3.86 (s, 3 H, OCH3), 4.33-4.39 (m, 2 H, NCH2Hb, CHOTIPS), 4.56 (d, J 6.4, 1 H, CHCHOTIPS), 6.60 (s, 1 H, ArH), 6.99(s, 1 H, ArH); δC (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_{4}Si requires [M+H]+, 420.2570. Minor product 70: oil; more polar; [α]_D^{23} +112 (c 2.80, CHCl₃); ν_max. (CHCl₃)/cm⁻¹ 2943, 2867, 1683, 1604, 1464, 1364, 1120, 883; δ_H (400 MHz, CDCl₃)
0.81-1.18 (m, 21 H, SiCH(CH₃)₂), 2.49 (d, J 16.0, 1 H, NCOCH₂H₃B), 2.62 (dd, J 16.0, 2.0, 1 H, ArCH₂H₃B), 2.70-2.89 (m, 3 H, ArCH₂H₃B, NCH₂H₃B, COCH₂H₃B), 3.86 (s, 3 H, OCH₃), 3.87 (s, 3 H, OCH₃), 4.42 (ddd, J 12.5, 5.5, 1.5, 1 H, CH₂H₃N), 4.80 -4.83 (m, 2 H, CHCHOTIPS), 6.63 (s, 2 H, ArH); δ_C (100.6 MHz, CDCl₃) 12.5 (SiCH), 17.7 (CH₃), 17.8 (CH₃), 29.0 (ArCH₂), 37.2 (NCH₂), 43.2 (NCOCH₂), 55.8 (OCH₃), 56.1 (OCH₃), 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_{4}Si 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 CH₃CN (4 mL) and water (1 mL). A solution of PhSeCl (51 mg, 0.27 mmol) in CH₃CN (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 Na₂CO₃ solution (5 mL), water (5 mL) and brine (5 mL). The organic phase was then dried over MgSO₄ 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: \( \nu_{\text{max.}} \) (CHCl\(_3\))/cm\(^{-1}\) 3518, 2936, 1682, 1362, 1360, 1110; \( \delta_\text{H} \) (400 MHz, CDCl\(_3\)) 1.20-1.50 (m, 3.3 H, CH\(_2\)), 1.90-2.30 (m, 3.3 H, CH\(_2\)), 2.90-3.20 (m, 8.5 H, CHHN, CH\(_2\)Ar, CH\(_2\)SeAr), 3.58 (m, 1.7 H, CHO\(_{H}\)), 3.80-3.83 (s, 10 H, OCH\(_3\)), 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); \( \delta_\text{C} \) (100 MHz, CDCl\(_3\)) 29.8 (CH\(_2\)), 29.9 (CH\(_2\)), 34.3 (CH\(_2\)), 34.6 (CH\(_2\)), 34.8 (CH\(_2\)), 36.4 (CH\(_2\)), 36.8 (CH\(_2\)), 55.8 (OCH\(_3\)), 56.1 (OCH\(_3\)), 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. C\(_{24}\)H\(_{27}\)NO\(_4\)Se 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 Ph\(_3\)SnH (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; \( \nu_{\text{max.}} \) (CHCl\(_3\))/cm\(^{-1}\) 3605, 2936, 2253, 1682, 1124, 903; \( \delta_\text{H} \) (400
MHz, CDCl₃, major diastereomer) 1.49-1.61 (m, 2 H, CCH₃H₅, CH₃H₅COH), 1.67-1.73 (m, 1 H, CH₂H₅COH), 1.84-1.88 (m, 1 H, CCH₃H₅), 2.12-2.35 (m, 4 H, NCOCH₂, CH₃H₅COHCH₃H₅), 2.56-2.60 (m, 1 H, ArCH₃H₅), 2.67-2.69 (m, 1 H), 3.03-3.10 (m, 1 H, ArCH₃H₅), 3.17-3.25 (m, 1 H, CH₃H₅N), 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, NCH₂H₅), 6.54 (s, 1 H, ArH), 6.65 (s, 1 H, ArH); δC (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.

(4aR,13bR)-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); νmax. (CHCl₃)/cm⁻¹ 2937, 1716, 1681, 1463, 1362, 1122; δH (500 MHz, CDCl₃) 2.10-2.16 (m, 1 H, 5-HA),
2.24-2.35 (m, 3 H, 1-H, 2-H\textsubscript{A}), 2.38-2.43 (m, 1 H, 2-H\textsubscript{B}), 2.60-2.76 (m, 3 H, 4-H\textsubscript{A}, 5-H\textsubscript{B}, 9-H\textsubscript{A}), 2.96-3.11 (m, 4 H, 4a-H, 4-H\textsubscript{B}, 8-H\textsubscript{A}, 9-H\textsubscript{B}), 3.86 (s, 3 H, OCH\textsubscript{3}), 3.88 (s, 3 H, OCH\textsubscript{3}), 4.32-4.40 (m, 1 H, 8-H\textsubscript{B}), 6.58 (s, 1 H, ArH), 6.69 (s, 1 H, ArH); \(\delta\)\textsubscript{C} (125 MHz, CDCl\textsubscript{3}) 27.6 (ArCH\textsubscript{2}), 33.6 (C\textsubscript{C}H\textsubscript{2}), 34.8 (CH\textsubscript{2}CH\textsubscript{2}CO), 35.3 (NCH\textsubscript{2}), 37.5 (CCH), 37.8 (NCOCH\textsubscript{2}), 43.3 (COCH\textsubscript{2}CH), 56.0 (OCH\textsubscript{3}), 56.4 (OCH\textsubscript{3}), 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]\textsuperscript{+}, 100), 338.1 ([M+Na]\textsuperscript{+}, 74); HRMS (ESI) found [M+H]\textsuperscript{+}, 316.1554. C\textsubscript{18}H\textsubscript{21}NO\textsubscript{4} requires [M+H]\textsuperscript{+}, 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 AlCl\textsubscript{3} (600 mg, 0.66 mmol) in Et\textsubscript{2}O (3 mL) was added dropwise to the solution of LiAlH\textsubscript{4} (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% NH\textsubscript{3}H\textsubscript{2}O (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 MgSO\textsubscript{4} 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: \([\alpha]_D^{27} +42\) (c 1.78, CHCl\textsubscript{3}); \(\nu\text{max.} (\text{CHCl}_3)/\text{cm}^{-1}\) 2937, 2866, 1638, 1463, 1358, 1096, 998; \(\delta\)\textsubscript{H} (400 MHz, CDCl\textsubscript{3}) 0.84-0.93 (m, 21 H, CH(CH\textsubscript{3})\textsubscript{2}), 1.52-1.88 (m, 4 H, CH\textsubscript{2}CH\textsubscript{A}H\textsubscript{B}CH=, CH\textsubscript{A}H\textsubscript{B}CHOSi), 2.08-2.19 (m, 2 H, CH\textsubscript{A}H\textsubscript{B}CH=, CH\textsubscript{A}H\textsubscript{B}CHOSi), 2.54-2.72 (m, 2 H, ArCH\textsubscript{2}), 2.92-3.26 (m, 4 H, CH\textsubscript{2}NCH\textsubscript{2}), 3.81 (s, 3 H, OCH\textsubscript{3}), 3.83 (s, 3 H, OCH\textsubscript{3}), 4.38 (dd, J 5.0, 2.5, 1 H, CHOSi), 4.82-4.91(m, 2 H, =CH\textsubscript{2}), 5.68-5.77 (m, 1 H,
(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. [α]D²⁷ +37 (c 1.20, CHCl₃); ν max. (CHCl₃)/cm⁻¹ 3563, 2937, 2836, 1639, 1609, 1463, 1358, 1096, 998; δH (400 MHz, CDCl₃) 1.58-1.64 (m, 2 H, CH₂H₃CH₂H₂CH=), 1.72-1.80 (m, 1 H, CH₂H₃CH₂CH=), 1.91-2.02 (m, 1 H, CH₂H₃CHOH), 2.10-2.23 (m, 2 H, CH₂H₃CH=, CH₂H₃CHOH), 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, CH₂H₃CHOH), 4.86 (dd, J 10.0, 1.6, 1 H, =CH₂H₃), 4.90 (dd, J 17.2, 1.6, 1 H, =CH₂H₃), 5.68-5.78 (m, 1 H, CH=), 6.65 (s, 1 H, ArH), 6.68 (s, 1 H, ArH); δC (100 MHz, CDCl₃) 27.6
(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 CH$_2$Cl$_2$ (3 mL) at $-78 \, ^\circ$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 CH$_2$Cl$_2$ (3 mL) was added dropwise. The resulting reaction mixture was then stirred at $-78 \, ^\circ$C for 2 h. Et$_3$N (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 CH$_2$Cl$_2$ (100 mL). The organic phase was washed with brine (10 mL), dried over anhydrous MgSO$_4$ 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. [$\alpha$]$_D^{23}$ $-$44 ($c$ 1.30, CHCl$_3$; $\nu$$_{\max}$ (CHCl$_3$)/cm$^{-1}$ 2936, 2850, 1756, 1608, 1463, 1358, 1119, 1104; $\delta$$_H$ (400 MHz, CDCl$_3$) 1.74-1.90 (m, 2 H, CCH$_2$), 2.02-2.24 (m, 2 H, CH$_2$CH$=$), 2.36-2.42 (m, 3 H, NCH$_2$H$_3$CH$_2$CO), 3.03-3.29 (m, 5 H, ArCH$_2$, CH$_2$NCH$_2$H$_3$), 3.84 (s, 3 H, OCH$_3$), 3.87 (s, 3 H, OCH$_3$), 4.90 (dd, $J$ 10.0, 1.6, 1 H, =CH$_2$H$_3$), 4.96 (dd, $J$ 17.2, 1.6, 1 H, =CH$_2$H$_3$), 5.70-5.84 (m, 1 H, CH$=$), 6.51 (s, 1 H, ArH), 6.95 (s, 1 H, ArH); $\delta$$_C$ (100 MHz, CDCl$_3$) 21.0 (CH$_2$), 29.3 (CH$_2$), 36.4 (CH$_2$), 38.0 (CH$_2$), 41.5 (CH$_2$), 43.6 (CH$_2$), 55.8 (OCH$_3$), 55.9 (OCH$_3$), 68.4 (C), 109.7 (ArCH), 111.6 (ArCH), 114.4 (CH$_2$=), 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. C$_{18}$H$_{25}$NO$_3$ requires [M+H], 302.1756.
(1S,10bR)-8,9-Dimethoxy-10b-(3-oxobutyl)-1-(triisopropylsilyloxy)-1,2,5,6-tetrahydropyrrolo[2,1-a]isoquinolin-3-one

PdCl$_2$ (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 O$_2$ 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 MgSO$_4$ 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 $[\alpha]_D^{26} -79$ (c 1.60, CHCl$_3$); $\nu$$_{max}$. (CHCl$_3$)/cm$^{-1}$ 2936, 2868, 1714, 1682, 1457, 1361, 1113, 1069, 996, 883; $\delta$$_H$ (400 MHz, CDCl$_3$) 1.05-1.10 (m, 21 H, CH(CH$_3$)$_2$), 2.00 (s, 3 H, CH$_3$CO), 2.18-2.24 (m, 3 H, COCH$_2$H$_6$CH$_2$), 2.54-2.78 (m, 5 H, ArCH$_2$, CH$_2$CON, COCH$_2$H$_6$CH$_2$), 2.85 (td, $J$ 12.8, 4.0, 1 H, NCH$_2$H$_9$), 3.75 (s, 3 H, OCH$_3$), 3.77 (s, 3 H, OCH$_3$), 4.31 (dd, $J$ 12.8, 5.0, 1 H, NCH$_2$H$_9$), 4.41 (t, $J$ 9.6, 1 H, CHOTIPS), 6.48 (s, 1 H, ArH), 6.80 (s, 1 H, ArH); $\delta$$_C$ (100.6 MHz, CDCl$_3$) 12.4 (SiCH), 17.6 (CH$_3$), 17.7 (CH$_3$), 17.8 (CH$_3$), 17.9 (CH$_3$), 28.2 (ArCH$_2$), 29.8 (COCH$_3$), 30.0 (CCH$_2$), 34.9 (ArCH$_2$CH$_2$), 38.9 (CH$_2$COMe), 40.6 (NCOCH$_2$), 55.6 (OCH$_3$), 55.7 (OCH$_3$), 66.2 (C), 75.9 (CHO$_2$), 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. C$_{27}$H$_{43}$NO$_5$Si requires [M+H$^+$], 490.2989.

(1S,10bS)-10b-(3-Hydroxybutyl)-8,9-dimethoxy-1,2,3,5,6,10b-hexahydro-
pyrrolo[2,1-\textit{a}]isoquinolin-1-ol 79

A solution of AlCl$_3$ (1.5 g, 11 mmol) in Et$_2$O (10 mL) was added dropwise to the solution of LiAlH$_4$ (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 MgSO$_4$ 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. $\nu_{\text{max.}}$ (CHCl$_3$/cm$^{-1}$) 3617, 3362, 2936, 2835, 1612, 1463, 1356, 1109, 866; $\delta_H$ (400 MHz, CDCl$_3$) 1.06 (d, $J$ 6.4, 3 H, CH$_3$), 1.12 (d, $J$ 6.4, 3 H, CH$_3$), 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, OCH$_3$), 3.85 (s, 3 H, OCH$_3$), 3.87 (s, 3 H, OCH$_3$), 3.88 (s, 3 H, OCH$_3$), 4.29-4.36 (m, 2 H, CHOHCH$_3$), 6.54 (s, 1 H, ArH), 6.57 (s, 1 H, ArH), 6.83 (s, 1 H, ArH), 6.92 (s, 1 H, ArH); $\delta_C$ (100 MHz, CDCl$_3$) 23.5 (CH$_3$), 24.0 (CH$_3$), 24.3 (CH$_2$), 27.0 (CH$_2$), 31.7 (CH$_2$), 31.8 (CH$_2$), 32.0 (CH$_2$), 32.1 (CH$_2$), 33.9 (CH$_2$), 34.5 (CH$_2$), 45.0 (CH$_2$), 47.7 (CH$_2$), 47.8 (CH$_2$), 48.9 (CH$_2$), 55.8 (OCH$_3$), 56.2 (OCH$_3$), 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]$^+$, 322.208. C$_{18}$H$_{27}$NO$_4$ requires [M+H]$^+$, 322.2018.

(R)-8,9-Dimethoxy-10b-(3-oxobutyl)-2,3,5,6-tetrahydropyrrolo[2,1-\textit{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 CH$_2$Cl$_2$ (2 mL) at $-78 \degree C$ 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 CH$_2$Cl$_2$ (2 mL) was added dropwise. The resulting reaction mixture was then stirred at $-78 \degree C$ for 2 hours, and then Et$_3$N (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 CH$_2$Cl$_2$ (30 mL). The organic phase was washed with water (5 mL), brine (5 mL), dried over anhydrous MgSO$_4$ 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%): $[\alpha]_D^{25} +50$ (c 0.75, CHCl$_3$); $\nu_{\text{max}}$ (CHCl$_3$)/cm$^{-1}$ 2936, 2850, 1746, 1709; $\delta_H$ (400 MHz, CDCl$_3$) 2.11 (s, 3 H, CH$_3$CO), 2.11-2.26 (m, 3 H, CH$_2$CH$_A$H$_B$), 2.35-2.43 (m, 3 H, CH$_2$CO, ArCH$_A$H$_B$), 2.48-2.54 (m, 1 H, CH$_2$CH$_A$H$_B$), 3.00-3.10 (m, 4 H, ArCH$_A$H$_B$CH$_A$H$_B$NCH$_2$), 3.14-3.22 (m, 1 H, ArCH$_2$CH$_A$H$_B$N), 3.82 (s, 3 H, OCH$_3$), 3.84 (s, 3 H, OCH$_3$), 6.51 (s, 1 H, ArH), 6.90 (s, 1 H, ArH); $\delta_C$ (100 MHz, CDCl$_3$) 21.1 (CH$_2$), 30.2 (CH$_3$), 32.6 (CH$_2$), 36.3 (CH$_2$), 39.2 (CH$_2$), 41.3 (CH$_2$), 43.5 (CH$_2$), 55.8 (OCH$_3$), 55.9 (OCH$_3$), 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. C$_{18}$H$_{23}$NO$_4$ requires [M$^+$+Na$^-$], 340.1515.

(S)-11,12-Dimethoxy-1,2,5,6,8,9-hexahydroindo[1-$\alpha$]isoquinolin-3-one (+)-2

![Chemical Structure](image-url)
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 CH$_2$Cl$_2$ (20 mL). The organic phase was washed with water (5 mL), brine (5 mL) and dried over anhydrous MgSO$_4$. After filtration and concentration, the crude product was purified by flash silica chromatography (eluent: CH$_2$Cl$_2$/MeOH = 10/1) to give a yellow oil (+)-2 (15.9 mg, 50%): [α]$_D^{26}$ +316 (c 0.40, CHCl$_3$); $\nu$$_{max}$ (CHCl$_3$)/cm$^{-1}$ 2936, 2852, 1666, 1463, 1360, 1107; δ$_H$ (400 MHz, CDCl$_3$) 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, OCH$_3$), 3.88 (s, 3 H, OCH$_3$), 6.12 (s, 1 H, 4-H), 6.56 (s, 1 H, ArH), 6.66 (s, 1 H, ArH); δ$_C$ (100 MHz, CDCl$_3$) 21.5 (9-CH$_2$), 28.6 (5-CH$_2$), 32.8 (2-CH$_2$), 35.9 (1-CH$_2$), 40.1 (8-CH$_2$), 45.7 (6-CH$_2$), 55.9 (OCH$_3$), 56.0 (OCH$_3$), 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. C$_{18}$H$_{21}$NO$_3$ requires [M+H]$^+$, 300.1594.