Supporting Information

**Total Synthesis of the Putative Structure of Stemonidine: The Definitive Proof of Misassignment**

Francisco Sánchez-Izquierdo, Pilar Blanco, Félix Busqué, Ramón Alibés, Pedro de March, Marta Figueredo,* Josep Font, and Teodor Parella†

*Departament de Química, Universitat Autònoma de Barcelona 08193 Bellaterra, Spain
†Servei de Ressonància Magnètica Nuclear, Universitat Autònoma de Barcelona.

marta.figueredo@uab.es

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General Procedures. Commercially available reagents were used as received. The solvents were dried by distillation over the appropriate drying agents. All reactions were performed avoiding moisture by standard procedures and under nitrogen atmosphere and monitored by analytical thin-layer chromatography (TLC) using silica gel 60 F254 pre-coated aluminum plates (0.25 mm thickness). Flash column chromatography was performed using silica gel 60 Å, particle size 35-70 µm. 1HNM R spectra were recorded on Bruker DPX250 (250 MHz), Bruker DPX360 (360 MHz), Bruker ARX400 (400 MHz), and Bruker AVANCE500 (500 MHz) spectrometers. Proton chemical shifts are reported in ppm (δ) (CDCl3 δ 7.26 ppm). 13CNMR spectra were recorded on Bruker DPX250 (62.5 MHz), Bruker DPX360 (90 MHz), Bruker ARX400 (100 MHz) and Bruker AVANCE500 (125 MHz) spectrometers with complete proton decoupling. Carbon chemical shifts are reported in ppm (δ) (CDCl3, δ 77.0). NMR signals were assigned with the help of PENDANT, COSY, HSQC, HMBC, and NOESY experiments. Infrared spectra were recorded on a Sapphire-ATR Spectrophotometer; peaks are reported in cm⁻¹. Optical rotation values were measured on an UV-vis Jasco J-175. High resolution mass spectra (HRMS) were recorded at Micromass-AutoSpec using (CI+). Enantiomeric purity of compound 4 was determined by CHPLC on a Waters 2690 chromatograph using a Daicel Chiralpak AD-H 4.6 x 250 mm column (PrOH/hexanes, 1/99; 0.8 mL·min⁻¹).

(S)-2-tert-Butyldiphenylsilyloxyethyl-3,4-dihydro-2H-pyrrole 1-oxide (6)

NaHCO3 (5.70 g, 67.9 mmol) was added to a stirred solution of amine 9 (4.60 g, 13.6 mmol) in a mixture of acetonitrile-THF (4:1, 25 mL) and Na2EDTA (0.01 M, 19 mL). The mixture was then cooled in an ice bath and Oxone® (8.76 g, 14.3 mmol) was added portionwise over 2 h. The mixture was stirred at 0 ºC for 20 min and then diluted with EtOAc (25 mL). The two phases were separated and the aqueous one was extracted with CH2Cl2 (3x40 mL). The combined organic extracts were dried over anhydrous MgSO4 and concentrated under reduced pressure to afford a yellow oil identified as a 1.3:1 mixture of nitrones 6 and 10 (4.30 g, 12.2 mmol, 90% yield). The
ratio **6:10** was determined by $^1$H-NMR. Pure samples of both nitrone **10** (first eluted) and **6** (second eluted) can be obtained by flash chromatography (CHCl₃/MeOH 40:1).

**10**: $^1$H NMR (250 MHz, CDCl₃): $\delta$ 7.62 (m, 4H), 7.38 (m, 6H), 4.67 (m, 2H:H1'), 3.94 (m, 2H:H2'), 2.86 (m, 2H:H4), 2.08 (m, 2H:H3'), 1.07 (s, 9H:C(CH₃)₃);

$^{13}$C-NMR (62.5 MHz, CDCl₃): $\delta$ 148.6 (C5), 135.4 (CPh), 132.4 (CPh), 129.9 (CPh), 127.7 (CPh), 62.6 (C1'), 59.7 (C2), 29.5 (C4), 26.7 (C(CH₃)₃), 19.1 (C(CH₃)₃).

**6**: $[\alpha]_{D}^{20} = -13$ (c 1.56, CH₂Cl₂), IR (ATR): 3070, 3048, 2930, 2856, 1587, 1471, 1462, 1427, 1245, 1205, 1111, 1082, 1034, 1009; $^1$H NMR (250 MHz, CDCl₃): $\delta$ 7.66 (m, 4H), 7.40 (m, 6H), 6.98 (bs, 1H:H5), 4.41 (dd, $J = 10.8$, 2.3 Hz, 1H:H1'), 3.69 (bs, 1H:H2), 3.99 (m, 1H:H 2), 3.69 (bd, $J = 10.8$ Hz, 1H:H1'), 2.70 (m, 2H:H4), 2.33 (m, 2H:H3), 1.04 (s, 9H:C(CH₃)₃);

$^{13}$C-NMR (62.5 MHz, CDCl₃): $\delta$ 135.3 (C5), 135.1 (CPh), 133.1 (CPh), 129.6 (CPh), 127.6 (CPh), 73.6 (C2), 62.0 (C1'), 27.3 (C4), 26.6 (C(CH₃)₃), 21.2 (C3), 19.1 (C(CH₃)₃); HRMS (Cl+): calcd for C₂₃H₂₇NNaO₂Si: 376.1703 [M+Na]+; found 376.1691.

**Methyl (2S,3R,3aS,6S)-6-(tert-butyldiphenylsilyloxy)methyl-2-(2-methoxycarbonyl)ethylperhydropyrrolo[1,2-b]isoxazole-3-carboxylate (4) and its (2S,3R,3aS,6S) isomer (11)**

A solution of nitrone **6** (1.00 g, 2.83 mmol) and olefin **5** (536 mg, 3.12 mmol) in toluene (15 mL) was heated at reflux for 10 h. Removal of the solvent and flash chromatography of the crude material (hexanes/EtOAc 4:1) afforded the following fractions: i) recovered **5** (31 mg, 0.18 mmol) as an oil; ii) exo adduct **11** (71 mg, 0.14 mmol, 5% yield) as an oil; and iii) endo adduct **4** (1.160 g, 2.21 mmol, 78% yield) as an oil.

**11**: $[\alpha]_{D}^{20} = -48$ (c 1.60, CH₂Cl₂), IR (ATR): 3071, 3049, 2951, 2931, 2857, 1736, 1461, 1428, 1360, 1262, 1198, 1169, 1110, 1007; $^1$H NMR (360 MHz, CDCl₃): $\delta$ 7.66 (m, 4H), 7.39 (m, 6H), 4.13 (dt, $J = 8.4$, 4.0 Hz, 1H:H2), 3.97 (q, $J \approx 6.4$ Hz, 1H:H3a), 3.77 (dd, $J = 9.8$, 4.5 Hz, 1H:H1'), 3.71 (s, 3H:OCH₃), 3.66 (s, 3H:OCH₃), 3.54 (dd, $J = 9.8$, 7.2 Hz, 1H:H1'), 3.47 (m, 1H:H6), 2.76 (dd, $J = 8.7$, 5.9 Hz, 1H:H3), 2.44 (m, 2H:H2'), 2.13 (m, 3H:H4, H5, H1'), 1.82 (m, 3H:H4, H5, H1'),...
1.05 (s, 9H:C(CH3)3); 13C NMR (90 MHz, CDCl3): δ 173.4 (CO2CH3), 171.6 (CO2CH3), 135.6 (CPh), 133.5 (CPh), 133.4 (CPh), 129.6 (CPh), 127.6 (CPh), 80.4 (C2), 69.4 (C3a), 69.1 (C6), 65.5 (C1''), 58.7 (C1), 52.2 (CO2CH3), 51.6 (CO2CH3), 30.6 (C2'), 30.0 (C4), 28.6 (C1'), 26.9 (C3), 26.8 (C(CH3)3), 19.2 (C(CH3)3); HRMS (CI+): calcd for C29H39NNaO6Si: 548.2439 [M+Na]+; found 548.2424.

4: [α]D20 = -90 (c 2.06, CH2Cl2); IR (ATR): 3070, 3048, 2951, 2878, 1737, 1429, 1362, 1173, 1112;
1H NMR (360 MHz, CDCl3): δ 7.66 (m, 4H), 7.42 (m, 6H), 4.18 (ddd, J = 9.3, 8.2, 3.8 Hz, 1H:H2), 3.98 (bq, J ≈ 8.1 Hz, 1H:H3a), 3.86 (dd, J = 10.1, 4.8 Hz, 1H:H1''), 4.09 (s, 3H:CO2CH3), 3.65 (s, 3H:CO2CH3), 3.60 (dd, J = 10.1, J = 7.3 Hz, 1H:H1''), 3.25 (m, 1H:H6), 3.13 (t, J = 9.3 Hz, 1H:H3), 2.42 (m, 2H:H2'), 2.05 (m, 2H:H5, H1'), 1.85 (m, 2H:H4, H1'), 1.53 (m, 2H:H4, H3), 1.05 (s, 9H:C(CH3)3); 13C NMR (90 MHz, CDCl3): δ 173.5 (CO2CH3), 170.7 (CO2CH3), 135.60 (CPh), 135.58 (CPh), 133.7 (CPh), 133.6 (CPh), 129.58 (CPh), 129.56 (CPh), 127.59 (CPh), 127.58 (CPh), 75.4 (C2), 68.8 (C6), 66.6 (C1''), 66.2 (C3a), 56.1 (C3), 51.9 (CO2CH3), 51.6 (CO2CH3), 30.5 (C2'), 27.34 (C5/C1'), 27.33 (C5/C1'), 27.0 (C6), 26.8 (C(CH3)3), 19.2 (C(CH3)3); HRMS (CI+): calcd for C29H39NNaO6Si: 548.2439 [M+Na]+; found 548.2424.

Methyl (3S,8S,9aR,9aS)-3-(tert-butyldiphenylsilyloxy)methyl-8-hydroxy-5-oxoperhydro-1H-pyrrolo[1,2-a]azepine-9-carboxylate (3)
Methyl (3S,9aS)-3-(tert-butyldiphenylsilyloxy)methyl-5-oxo-2,3,5,6,7,9a-hexahydro-1H-pyrrolo[1,2-a]azepine-9-carboxylate (12)

To a solution of alcohol 3 (1.67 g, 3.37 mmol), PPh3 (1.15 g, 4.39 mmol), and benzoic acid (0.54 g, 4.39 mmol) in anhydrous THF (30 mL), DIAD (0.86 mL, 4.39 mmol) was slowly added. TLC analysis of the reaction mixture (EtOAc) showed that starting 2 was consumed after 1.5 h. The organic solvent was removed under vacuum and the resulting oil was purified by flash column chromatography on silica gel (EtOAc:hexanes 2:1) to afford 12 (1.42 g, 2.97 mmol, 88% yield): $R_f = 0.58$ (EtOAc); $[\alpha]_D^{20} = -159$ (c 0.78, CH2Cl2); IR (ATR): 2931, 2856, 1714, 1644, 1427, 1254, 1216, 1105; $^1H$ NMR (250 MHz, CDCl3): $\delta$ 7.63 (m, 4H), 7.37 (m, 6H), 6.68 (m, 1H:H₈), 4.86 (m, 1H:H₉a), 4.30 (m, 1H:H₃), 3.86 (m, 2H:2H₁₉), 3.73 (s, 3H, CO₂CH₃), 2.67 (qd, $J = 13.6$, 4.4 Hz, 1H:H₀), 2.48 (m, 4H:H₁, H₆, 2H₇), 1.91 (m, 3H:H₁, 2H₂), 1.06 (s, 9H:CH₃); $^{13}C$ NMR (62.5 MHz, CDCl3): $\delta$ 172.2 (CO₂CH₃), 168.7 (C₅), 139.2 (C₈), 135.2 (C₆), 135.0 (C₉), 133.6 (C₉a), 133.5 (C₈), 129.6 (C₉b), 127.6 (C₈b), 126.9 (C₆b), 126.9 (C₅b), 63.6 (C₉a), 54.9 (C₉), 60.1 (C₈), 57.0 (C₉a), 52.0 (OCH₃), 33.9 (C₆), 31.7 (C₁), 27.6 (C₇), 26.9 (C(CH₃)₃), 25.5 (C₂), 19.2 (C(CH₃)₃); HRMS (CI+): calcd for C₂₈H₃₇NO₄Si: 496.2514 [M+H]⁺; found 496.2512.
Methyl (3S,8R,9S,9aS)-3-(tert-butyldiphenylsilyloxy)methyl-8,9-dihydroxy-5-oxooctahydro-1H-pyrrolo[1,2-a]azepine-9-carboxylate (13)

NMO (400 mg, 3.42 mmol) and OsO₄ (2.5% in ¹BuOH, 1.3 mL, 0.11 mmol) were added to a solution of olefin 12 (1.26 g, 2.63 mmol) in acetone:water (9:1, 25 mL) at 60 ºC. TLC analysis of the reaction mixture showed that starting 12 was consumed after 1.5 h. The reaction mixture was quenched by addition of NaHSO₃, the organic solvent was evaporated under vacuum, and the aqueous layer was extracted with CH₂Cl₂ (4x7 mL). The combined organic extracts were dried over anhydrous MgSO₄ and concentrated. The yellowish oily residue was purified by flash column chromatography on silica gel to furnish 13 (1.24 g, 2.42 mmol, 92% yield) as a colorless oil: Rᵋ = 0.33 (EtOAc); [α]D²⁰ = -59 (c 2.06, CH₂Cl₂); IR (ATR): 3323, 2930, 2856, 1728, 1616, 1427, 1237, 1105; ¹H NMR (360 MHz, CDCl₃): δ 7.60 (m, 4H), 7.37 (m, 6H), 4.34 (d, J = 8.8 Hz, 1H:H⁹a), 4.09 (m, 1H:H₃), 3.97 (s, 1H:OH), 3.86 (m, 1H:H₈), 3.82 (dd, J = 9.9, 3.1 Hz, 1H:H¹₀), 3.80 (s, 3H:CO₂CH₃), 3.73 (dd, J = 9.9, 5.9 Hz, 1H:H¹₀), 2.95 (m, 2H:H₆, OH), 2.21 (m, 3H:H₁, H₆, H₇), 1.98 (m, 3H:H₁, H₂, H₇), 1.46 (m, 1H:H₂), 1.04 (s, 9H:C(CH₃)₃); ¹³C NMR (90 MHz, CDCl₃): δ 174.2 (CO₂CH₃), 173.1 (C₅), 135.6 (Cₙ₈), 135.56 (Cₙ₉), 135.54 (Cₙ₉), 135.33 (Cₙ₉), 135.31 (Cₙ₉), 129.7 (Cₙ₉), 127.7 (Cₙ₉), 81.7 (C₉), 71.8 (C₈), 135.54 (Cₙ₉), 63.3 (C₉), 60.0 (C₅), 58.8 (Cₙ₉), 53.9 (CO₂CH₃), 30.6 (C₆), 26.9 (C(CH₃)₃), 26.1 (C₇), 25.6 (C₁), 25.0 (C₂), 19.3 (C(CH₃)₃); MS (ESI, MeCN) m/z 534 (MNa⁺); Anal. Caled for C₂₈H₃₇NO₆Si: C, 65.72; H, 7.29; N, 2.74. Found: C, 65.44; H, 7.39; N, 2.66.

Methyl (3S,8R,9S,9aS)-3-(tert-butyldiphenylsilyloxy)methyl-9-hydroxy-8-methoxy-5-oxooctahydro-1H-pyrrolo[1,2-a]azepine-9-carboxylate (15)

To a solution of diol 13 (1.24 g, 2.42 mmol) in dry THF (25 mL) at 0 ºC, was added NaH (291 mg, 7.27 mmol) in small portions and over 30 min. After stirring 30 min at 0 ºC, Me₂SO₄ (230 µL, 2.42 mmol) was added, the reaction mixture was slowly warmed up to room temperature, and then
stirred overnight. The organic layer was washed with NH₄Cl (aqueous saturated solution) and the aqueous layer was then extracted with EtOAc (2x10 mL). The combined organic phases were dried over anhydrous MgSO₄ and concentrated under vacuum. Flash column chromatography of the resulting oil on silica gel (EtOAc:hexanes 4:1 to EtOAc) gave starting diol 13 (142 mg, 0.28 mmol, 11% yield) and 15 (940 mg, 1.79 mmol, 74% yield, 84% yield from unrecovered 13). 15: Rₜ = 0.44 (EtOAc); [α]ᵣ⁰₂⁰ = -76 (c 1.95, CH₂Cl₂); ¹H NMR (360 MHz, CDCl₃): δ 7.63 (m, 4H), 7.40 (m, 6H), 4.16 (m, 2H: H₃, H₉a), 3.80 (s, 3H:CO₂CH₃), 3.80 (m, 2H:2H₁₀), 3.61 (dd, J = 7.6, 2.6 Hz, 1H:H₈), 3.54 (s, 1H:OH), 3.37 (s, 3H:OCH₃), 2.75 (ddd, J = 14.4, 9.7, 6.0 Hz, 1H:H₆), 2.24 (m, 4H: 2H₁, H₆, H₇), 1.98 (m, 2H:H₂, H₇), 1.64 (m, 1H:H₂), 1.06 (s, 9H:C(CH₃)₃); ¹³C NMR (90 MHz, CDCl₃): δ 172.8 (CO₂CH₃), 171.8 (C₅), 135.5 (C₆), 133.52 (C₆), 133.5 (C₆), 129.6 (C₆), 127.62 (C₆), 127.61 (C₆), 81.1 (C₈), 78.0 (C₉), 63.2 (C₁₀), 61.3 (C₆), 59.9 (C₃), 57.6 (OCH₃), 52.9 (CO₂CH₃), 31.3 (C₆), 26.9 (C(CH₃)₃), 26.1 (C₁), 25.3(C₂), 20.8 (C₇), 19.2 (C(CH₃)₃); HRMS (CI⁺): calcd for C₂₉H₄₀NO₆Si: 526.2619 [M+H⁺]; found 526.2613.

(3S,8R,9S,9aS)-3-(tert-Butyldiphenylsilyloxy)methyl-9-hydroxy-9-hydroxymethyl-8-methoxy-octahydro-5H-pyrrolo[1,2-a]azepin-5-one (16)

A recently opened solution of LiBH₄ in THF (2M, 4.00 mL, 8.00 mmol) was added to a stirred solution of ester 15 (1.05 g, 2.00 mmol) in dry THF (20 mL) at room temperature. After 18 h, TLC analysis (EtOAc) of the reaction mixture showed no starting material. The excess of LiBH₄ was quenched with NH₄Cl saturated solution (CAUTION! To avoid a vigorous effervescence, NH₄Cl must be added very slowly). Then EtOAc was added, and the aqueous phase was extracted with CH₂Cl₂ (2x10 mL). The combined organic extracts were dried over anhydrous Na₂SO₄ and concentrated in vacuo. Flash column chromatography purification (EtOAc) afforded 16 (0.965 g, 1.97 mmol, 97% yield): Rₜ = 0.24 (EtOAc); [α]ᵣ⁰₂⁰ = -68 (c 1.32, CH₂Cl₂); IR (ATR): 3389, 2930, 2856, 1619, 1446, 1426, 1359, 1257, 1173, 1096; ¹H NMR (360 MHz, CDCl₃): δ 7.62 (m, 4H), 7.39 (m, 6H), 4.19 (m, 2H: H₃, H₉a), 3.79 (dd, J = 9.9, 3.2 Hz, 1H:H₁₀), 3.75 (dd, J = 9.9, 5.6 Hz, 1H:H₁₀), 3.71 (m, 1H:H₈), 3.64 (d, J = 11.8 Hz, 1H:H₁₁), 3.45 (m, 1H:H₁₁), 3.39 (s, 3H:OCH₃), 3.21
(d, $J = 1.7$ Hz, 1H:OH), 2.71 (bt, $J = 12.7$ Hz, 1H:H$_6$), 2.32 (m, 1H:H$_2$), 2.17 (m, 3H:H$_2$, H$_6$, H$_7$), 2.05 (m, 1H:PH), 1.98 (dd, $J = 13.1$, 8.2 Hz, 1H:H$_1$), 1.83 (m, 2H:H$_1$, H$_7$), 1.05 (s, 9H:C(CH$_3$)$_3$);

$^{13}$C NMR (90 MHz, CDCl$_3$): $\delta$ 173.1 (C$_5$), 135.51 (C$_{Ph}$), 135.49 (C$_{Ph}$), 133.6 (C$_{Ph}$), 133.4 (C$_{Ph}$), 129.62 (C$_{Ph}$), 129.58 (C$_{Ph}$), 127.63 (C$_{Ph}$), 127.60 (C$_{Ph}$), 79.3 (C$_8$), 75.6 (C$_9$), 63.0 (C$_{10}$), 61.3 (C$_{11}$), 60.1 (C$_3$), 58.7 (C$_{9a}$), 56.7 (OCH$_3$), 29.8 (C$_6$), 26.9 (C(CH$_3$)$_3$), 26.2 (C$_2$), 25.3 (C$_1$), 21.3 (C$_7$), 19.2 (C(CH$_3$)$_3$); HRMS (CI+): calc'd for C$_{28}$H$_{40}$NO$_5$Si: 498.2670 [M+H]$^+$; found 498.2671.

(3$S$,8$R$,9a$S$)-3-(tert-Butyldiphenylsilyloxy)methyl-8-methoxytetrahydro-1$H$-pyrrolo[1,2-$a$]azepine-$5,9(6$H$,9$aff$)$-dione (14)

A solution of diol 16 (1.28 g, 2.56 mmol) in dry THF (25 mL) was added to stirred suspension of Pb(OAc)$_4$ (1.71 g, 3.85 mmol) in dry THF (38 mL) at room temperature. After 1.5 h TLC analysis (EtOAc) of the reaction mixture revealed the absence of diol 16. The mixture was filtered through Celite®, the organic solvent was removed under vacuum and the resulting colorless oil was purified by flash column chromatography on silica gel (EtOAc:hexanes 1:1) to give ketone 14 (1.09 g, 2.35 mmol, 92% yield): $R_f = 0.52$ (EtOAc); [$\alpha$]$_D^{20} = -81$ (c 1.35, CH$_2$Cl$_2$); IR (ATR): 2931, 2857, 1731, 1620, 1427, 1189, 1105; $^1$H NMR (360 MHz, CDCl$_3$): $\delta$ 7.61 (m, 4H), 7.35 (m, 6H), 4.43 (dd, $J = 8.7$, 3.1 Hz, 1H:H$_{9a}$), 4.27 (m, 1H:H$_3$), 4.04 (dd, $J = 8.1$, 6.5 Hz, 1H:H$_8$), 3.90 (dd, $J = 10.2$, 5.2 Hz, 1H:H$_{10}$), 3.78 (dd, $J = 10.2$, 2.8 Hz, 1H:H$_{10}$), 3.31 (s, 3H:OCH$_3$), 2.60 (m, 1H:H$_6$), 2.36 (m, 3H:H$_2$, H$_6$, H$_7$), 2.07 (m, 3H:H$_1$, 2H$_2$), 1.91(m, 1H:H$_7$), 1.05 (s, 9H:C(CH$_3$)$_3$); $^{13}$C NMR (90 MHz, CDCl$_3$): $\delta$ 208.4 (C$_9$), 170.9 (C$_3$), 135.51 (C$_{Ph}$), 135.48 (C$_{Ph}$), 133.3 (C$_{Ph}$), 133.2 (C$_{Ph}$), 129.7 (C$_{Ph}$), 127.7 (C$_{Ph}$), 82.5 (C$_8$), 64.0 (C$_{9a}$), 63.4 (C$_{10}$), 59.5 (C$_3$), 57.7 (OCH$_3$), 31.7 (C$_6$), 28.6 (C$_1$), 28.2 (C$_7$), 26.9 (C(CH$_3$)$_3$), 26.6 (C$_2$), 19.2 (C(CH$_3$)$_3$); HRMS (CI+): calc'd for C$_{27}$H$_{36}$NO$_4$Si: 466.2408 [M+H]$^+$; found 466.2404.
(2R,3’S,8’R,9a’S)-3’-(tert-Butyldiphenylsilyloxy)methyl-8’-methoxy-4-methylenehexahydro-3H-spiro{furan-2,9’-pyrrolo[1,2-a]azepin}-5,5’(4H,6’H)-dione (18)

To a stirred solution of ketone 14 (1.09 g, 2.35 mmol) in dry THF (25 mL) under N₂ atmosphere, Zn (460 mg, 7.04 mmol) was added. The mixture was heated up and, when reflux started, a solution of ethyl 2-(bromomethyl)acrylate, 17, (486 µL, 3.52 mmol) in dry THF (12 mL) was added. After 1 h of heating at reflux, TLC analysis (Et₂O) revealed the absence of 14 in the reaction mixture. The mixture was filtered through Celite® and the organic solvent evaporated under vacuum. The remaining colorless oil was dissolved in CH₂Cl₂ (10 mL) and washed with NH₄Cl saturated solution. The aqueous phase was extracted with CH₂Cl₂ (2x5 mL). The combined organic layers were dried over anhydrous MgSO₄ and concentrated in vacuo. Purification of the crude material by flash column chromatography on silica gel (Et₂O) furnished lactone 18 (1.08 g, 2.01 mmol, 86% yield): Rₜ = 0.18 (Et₂O); [α]D²⁰ = -46 (c 0.5, CH₂Cl₂); ¹H NMR (360 MHz, CDCl₃): δ 7.60 (m, 4H), 7.38 (m, 6H), 6.26 (t, J = 2.9 Hz, 1H:H₆), 5.64 (t, J = 2.5 Hz, 1H:H₆), 4.26 (m, 1H:H₃’), 4.02 (d, J = 9.0 Hz, 1H:H₉’), 3.87 (dd, J = 10.0, 5.3 Hz, 1H:H₇’), 3.80 (dd, J = 10.0, 3.0 Hz, 1H:H₇’), 3.34 (s, 3H:OCH₃), 3.30 (dd, J = 8.2, 2.7 Hz, 1H:H₈’), 2.94 (dt, J = 18.1, 2.8 Hz, 1H:H₃’), 2.65 (m, 2H:H₃, H₆’), 2.32 (m, 2H:H₃, H₆’), 1.78 (m, 2H:H₃’, H₇’), 1.04 (s, 9H:C(CH₃)₃); ¹³C NMR (90 MHz, CDCl₃): δ 171.4 (C₅), 169.4 (C₅’), 135.53 (C₆), 135.51 (C₆’), 134.4 (C₄), 133.6 (C₇), 133.5 (C₆), 129.7 (C₈), 129.6 (C₉), 127.7 (C₈), 127.6 (C₉), 122.2 (C₆), 85.4 (C₇), 82.8 (C₂), 63.3 (C₃), 61.1 (C₉’), 59.9 (C₃’), 57.6 (OCH₃), 34.5 (C₅), 30.8 (C₇), 26.9 (C(CH₃)₃), 25.6 (C₂’), 26.1 (C₇’), 20.6 (C₇), 19.3 (C(CH₃)₃); HRMS (Cl⁺): calcd for C₃₁H₄₀NO₅Si: 534.2670 [M+H]⁺; found 534.2668.
A solution of Et$_3$N·3HF (6.6 mL, 40.3 mmol) was added to a stirred solution of 18 (1.08 g, 2.01 mmol) in dry THF (34 mL). The reaction mixture was heated at the reflux temperature for 4 h, when TLC analysis showed no starting material. The solution was concentrated under vacuum and the resulting oil was purified by flash column chromatography on silica gel (EtOAc to EtOAc:EtOH 1:1) to furnish alcohol 19 (515 mg, 1.74 mmol, 87% yield): $[\alpha]_D^{20} = -115$ (c 0.22, EtOH); $^1$H NMR (360 MHz, CDCl$_3$): $\delta$ 6.26 (t, $J = 3.0$ Hz, 1H:H$_6$), 5.67 (t, $J = 2.6$ Hz, 1H:H$_6$), 4.55 (m, 1H:OH), 4.23 (m, 2H:H$_3$, H$_{9a}$), 3.64 (m, 2H:2H$_1''$), 3.34 (s, 3H:OCH$_3$), 3.27 (dd, $J = 7.0$, 2.5 Hz, 1H:H$_8$), 2.92 (dt, $J = 18.3$, 2.9 Hz, 1H:H$_3$), 2.80 (ddd, $J = 15.0$, 10.5, 5.0 Hz, 1H:H$_6$), 2.73 (dt, $J = 18.3$, 2.5 Hz, 1H:H$_3$), 2.39 (ddd, $J = 14.4$, 5.8, 4.9 Hz, 1H:H$_6$), 2.02 (m, 4H: H$_1'$, H$_2'$, 2H$_7'$), 1.77 (m, 1H:H$_1'$), 1.56 (m, 1H:H$_2'$); $^{13}$C NMR (90 MHz, CDCl$_3$): $\delta$ 174.2 (C$_{5'}$), 169.2 (C$_5$), 133.9 (C$_4$), 122.9 (C$_6$), 84.3 (C$_2$), 82.5 (C$_8$), 66.7 (C$_{1''}$), 62.5 (C$_3$), 61.0 (C$_{9a}$), 57.4 (OCH$_3$), 35.0 (C$_3$), 30.5 (C$_6$), 27.3 (C$_2$), 26.0 (C$_1$), 20.5 (C$_7$); HRMS (Cl+): calcd for C$_{15}$H$_{22}$NO$_5$: 296.1492 [M+H]$^+$; found 296.1497.

A commercially available solution of the Dess-Martin periodinane in CH$_2$Cl$_2$ (15% wt, 1.85 mL, 0.89 mmol) was added via syringe to a solution of alcohol 19 (219 mg, 0.74 mmol) in dry CH$_2$Cl$_2$ (6.1 mL). After 2 h of stirring at room temperature, TLC analysis indicates the complete consumption of the starting material. The solution was washed with NaHCO$_3$ saturated solution
containing a sevenfold excess of Na$_2$S$_2$O$_3$, the aqueous phase was extracted with CH$_2$Cl$_2$ (2x5 mL), the combined organic extracts were dried over anhydrous Na$_2$SO$_4$ and concentrated in vacuo. Flash column chromatography on silica gel (EtOAc) of the resulting oil provided aldehyde 20 (200 mg, 0.68 mmol, 92% yield): $R_f$ 0.43 (EtOAc:MeOH 9:1); $[\alpha]_D^{20} = -149$ (c 0.65, CH$_2$Cl$_2$); $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 9.54 (d, $J = 1.5$ Hz, 1H:H$_{1''}$), 6.30 (t, $J = 3.0$ Hz, 1H:H$_6$), 5.71 (t, $J = 2.6$ Hz, 1H:H$_6$), 4.58 (m, 1H:H$_3'$), 4.34 (bd, $J = 8.24$ Hz, 1H:H$_{9a'}$), 3.37 (s, 3H:OCH$_3$), 3.33 (dd, $J = 6.3$, 2.4 Hz, 1H:H$_8'$), 2.96 (dt, $J = 18.4$, 2.9 Hz, 1H:H$_3$), 2.88 (ddd, $J = 14.9$, 10.5, 4.5 Hz, 1H:H$_{6}$), 2.76 (bd, $J = 18.4$ Hz, 1H:H$_3$), 2.40 (m, 1H:H$_{6'}$), 2.04 (m, 4H:H$_1'$, H$_2'$, 2H$_7'$), 1.85 (m, 2H:H$_1'$, H$_2'$); $^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ 198.1 (C$_{1''}$), 175.1 (C$_5'$), 169.1 (C$_5$), 133.7 (C$_4$), 123.4 (C$_6$), 83.7 (C$_2$), 89.5 (C$_8$), 66.1 (C$_3$), 59.8 (C$_9a$), 57.3 (OCH$_3$), 35.2 (C$_3$), 29.2 (C$_6$), 26.2/24.1 (C$_1}$/C$_2$), 20.7 (C$_7$); HRMS (Cl+): calcd for C$_{15}$H$_{20}$NO$_5$: 294.1336 [M+H]$^+$; found 294.1334.

(2$R$,3$'$S,8$'$R,9a$'$S,2$''$R)- and (2$R$,3$'$S,8$'$R,9a$'$S)-8'-Methoxy-4-methylene-3'-[(2$S$)-4-methylene-5-oxotetrahydrofuran-2-yl]hexahydro-3$'H$-spiro{furan-2,9'$'$-pyrrolo[1,2-a]azepine}-5,5'(4$H$, 6$'$$H$)-dione (21 and 22)

To a stirred solution of aldehyde 20 (460 mg, 1.57 mmol) in dry THF (16 mL) under N$_2$ atmosphere, Zn (308 mg, 4.71 mmol) was added. The solution was heated up and, when reflux started, a solution of ethyl 2-(bromomethyl)acrylate, 17, (325 µL, 2.35 mmol) in dry THF (8 mL) was added. After 1 h TLC analysis of the reaction mixture (EtOAc:MeOH 9:1) revealed the absence of starting aldehyde. The reaction mixture was filtered through Celite® and the organic solvent was evaporated under vacuum. The remaining colorless oil was purified by flash column chromatography on silica gel (EtOAc to EtOAc:MeOH 95:5) to provide the following fractions: i) bislactone erythro 21 (214 mg, 0.59 mmol, 38% yield); a mixture of 21 and its threo isomer 22 (46 mg, 0.13 mmol, 8% yield); iii) bislactone 21 (151 mg, 0.42 mmol, 27% yield).

21 (erythro): $^1$H NMR (360 MHz, CDCl$_3$): $\delta$ 6.25 (t, $J = 3.0$ Hz, 1H:H$_6$/H$_6$), 6.24 (t, $J = 3.0$ Hz, 1H:H$_6$/H$_6$), 5.66 (t, $J = 2.5$, 2H: H$_6$, H$_6$), 5.36 (ddd, $J = 8.0$, 6.2, 1.4 Hz, 1H:H$_{2''}$), 4.24 (m, 2H:H$_3'$,
A solution of lactam 21 (21 mg, 58.1 µmol) in dry THF (2 mL) was added to a flask containing Lawesson’s reagent (26 mg, 63.9 µmol) and the mixture was heated at reflux for 4.5 h. At this time, TLC analysis (EtOAc) of the reaction mixture showed no starting material. The solvent was

(2R,4S,3'S,8'R,9a'S,2''R,4''R)- and (2R,4R,3'S,8'R,9a'S)-8'-Methoxy-4-methyl-3'-[(2R,4R)-4-methyl-5-oxotetrahydrofuran-2-yl]hexahydro-3H-spiro[furan-2,9'-pyrrolo[1,2-a]azepine]-5(4H,6'H)-one (24)

![](image.png)
removed under vacuum and the resulting oil was filtered through Al₂O₃ Brockman I using EtOAc as eluent. Evaporation under reduced pressure of the organic solvent afforded a whitish solid (16 mg, Rₖ: 0.58). Raney-Ni (400 mg) was added to a solution of this solid in EtOH (2 mL) and the mixture was heated at reflux for 2 h. Then, the mixture was filtered through Celite® and the solvent was evaporated in vacuo. The residue was purified by flash column chromatography on silica gel (EtOAc:hexanes 1:4 to 1:1) to give a mixture of the amines 23 and 24 (11 mg, 31.3 µmol, 54% yield). By repeated chromatographies an enriched sample of 24 was isolated.

24: ¹H NMR (500 MHz, CDCl₃): δ 4.71 (ddd, J = 10.7, 5.9, 2.1 Hz, 1H:H₂''), 3.54 (d, J = 9.9 Hz, 1H:H₈''), 3.30 (s, 3H:OCH₃), 3.27 (bd, J = 7.5 Hz, 1H:H₅''), 3.19 (ddd, J = 12.2, 5.6, 2.2 Hz, 1H:H₅'), 2.98 (dd, J = 9.7, 2.3 Hz, 1H:H₉''), 2.88 (tq, J = 10.0, 7.4 Hz, 1H:H₄), 2.66 (m, 1H:H₄'), 2.59 (td, J = 12.2, 3.8 Hz, 1H:H₃'), 2.48 (dd, J = 13.0, 10.1, 1H:H₃), 2.35 (ddd, J = 12.7, 9.0, 5.9 Hz, 1H:H₃''), 2.13 (m, 1H:H₇'), 2.00 (m, 1H:H₂'), 1.82 (m, 2H:H₆', H₇'), 1.70 (m, 2H:H₉', H₆), 1.55 (m, 3H:H₁', H₇', H₃''), 1.28 (d, J = 7.1 Hz, 3H:3H₆''), 1.26 (m, 1H:H₃), 1.20 (d, J = 7.4 Hz, 3H:3H₆); ¹³C NMR (125 MHz, CDCl₃) δ 181.0 (C₅), 179.2 (C₅''), 91.0 (C₂), 87.6 (C₈), 76.9 (C₂''), 70.0 (C₉''), 66.5 (C₃), 57.5 (OCH₃), 51.1 (C₅'), 35.8 (C₄), 35.5 (C₄''), 35.3 (C₃), 34.2 (C₃''), 28.7 (C₆'), 26.8 (C₇), 25.6 (C₁'), 25.3 (C₂'), 16.8 (C₆), 15.2 (C₅'').

23: ¹H-NMR (500 MHz, CDCl₃, mixture of 23 and 24): see Figure below; ¹³C NMR (125 MHz, CDCl₃, data extracted from a mixture of 23 and 24) δ 180.8, 179.3, 91.4, 86.2, 69.9, 66.2, 57.3, 50.9, 35.4, 35.0, 34.1, 33.5, 27.8, 26.7, 25.6, 25.4, 16.4, 15.2.

(2R,4S,3’S,8’R,9a’S,2’’S,4’’R)- (25) and (2R,4R,3’S,8’R,9a’S)-8’-Methoxy-4-methyl-3’-[(2S,4R)-4-methyl-5-oxotetrahydrofuran-2-yl]hexahydro-3H-spiro{furan-2,9’-pyrrolo[1,2-a]-azepine}-5,5’(4H,6’’H)-dione (26)

To a solution of bislactone 22 (39 mg, 0.108 mmol) in a 9:1 mixture of EtOH and 2M HCl (3 mL), Pd/C (40 mg) was added. The reaction was stirred in a 6 bar atmosphere of H₂ for 23 h. Then, it was filtered through Celite® and the filtrate was washed with saturated solution of NaHCO₃. The
aqueous layer was extracted with CH$_2$Cl$_2$ (3x5 mL). The combined organic extracts were dried over anhydrous Na$_2$SO$_4$ and concentrated under reduced pressure. The residue was purified by flash column chromatography (EtOAc:hexanes 1:1 to 5:1) to give a mixture of lactones 25 and 26 (27 mg, 73.9 µmol, 68% yield): $^1$H NMR (500 MHz, CDCl$_3$): see Figure below.

$^{(2R,4R,3’S,8’R,9a’S)-8’-Methoxy-4-methyl-3’-[(2S,4S)-4-methyl-5-oxotetrahydrofuran-2-yl]}
$hexahydro-3H-spiro{furan-2,9’-pyrrolo[1,2-a]azepine}-5(4H,6’H)-one (2) and its (4S) epimer (epi-2)

Lawesson’s reagent (30 mg, 73.9 µmol) was added to a solution of a mixture of 25 and 26 (27 mg, 73.9 µmol) in dry THF (3 mL) and the mixture was heated at the reflux temperature for 4.5 h. At this time, TLC analysis (EtOAc) of the reaction mixture showed no starting lactam. The solvent was removed under vacuum and the residue was filtered through Al$_2$O$_3$ Brockman I using EtOAc as eluent. Evaporation of the solvent under vacuum afforded a white solid (20 mg), which was dissolved in EtOH (3 mL). Then Raney-Ni (400 mg) was added and the reaction mixture was heated at reflux for 2 h. Then, it was filtered through Celite® and the solvent was evaporated in vacuo. Purification of the residue by flash column chromatography on silica gel (EtOAc:hexanes 2:1) furnished a mixture of 2 and epi-2 (11 mg, 31.3 µmol, 45% yield for the two steps). Repeated column chromatography provided analytical samples of each diastereomer.

2: first eluted; [α]$_D^{20}$ = -16 (c 0.25, acetone), [α]$_D^{20}$ = -30 (c 0.25, CH$_2$Cl$_2$); IR (ATR): 2960, 2958, 2924, 2886, 2855, 2825, 1750, 1453, 1441, 1256, 1230, 1222, 1172, 1111, 1088, 1008; $^1$H NMR (500 MHz, CDCl$_3$): δ 4.31 (ddd, $J$ = 10.9, 8.2, 5.4 Hz, 1H:H$_{2''}$), 3.57 (m, 1H:H$_{5'}$), 3.55 (d, $J$ = 9.8 Hz, 1H:H$_8$), 3.31 (s, 3H:OCH$_3$), 3.28 (m, 1H:H$_{3'}$), 2.90 (m, 2H:H$_4$, H$_{9a'}$), 2.59 (m, 2H:H$_{5'}$, H$_{4''}$), 2.52 (dd, $J$ = 12.9, 10.1 Hz, 1H:H$_3$), 2.38 (ddd, $J$ = 12.8, 8.3, 5.4 Hz, 1H:H$_{3''}$), 2.05 (tt, $J$ = 12.4, 7.2 Hz, 1H:H$_2$), 1.74 (m, 5H:2H$_1$, 2H$_6$, H$_7$), 1.50 (m, 3H:H$_2$, H$_7$, H$_3'$), 1.26 (d, $J$ = 7.0 Hz, 3H:3H$_6$), 1.26 (m, 1H:H$_3$), 1.22 (d, $J$ = 7.4 Hz, 3H:3H$_6$), $^{13}$C NMR (125 MHz, CDCl$_3$) δ 180.8 (C$_5$), 179.5 (C$_{3''}$), 90.8 (C$_2$), 87.2 (C$_8$), 79.1 (C$_{2''}$), 69.3 (C$_4$), 68.5 (C$_{3'}$), 57.5 (OCH$_3$), 52.1 (C$_5$), 35.69
(C_3/C_9a/C_3\''), 35.67 (C_3/C_9a/C_3\'''), 35.60 (C_3/C_9a/C_3\'''), 34.8 (C_4\'''), 28.3 (C_6'), 26.9 (C_2', C_7'), 25.3 (C_1'), 16.8 (C_6), 14.8 (C_6''); HRMS (CI+): calcd for C_{19}H_{30}NO_5: 352.2118 [M+H]^+; found 352.2124.

**Epi-2:** second eluted; [α]_D\textsuperscript{20} = -60 (c 0.09, acetone); IR (ATR): 2959, 2928, 2851, 2823, 1757, 1450, 1375, 1334, 1320, 1260, 1236, 1155, 1115, 1008; \textsuperscript{1}H NMR (500 MHz, CDCl_3): δ 4.30 (ddd, J = 10.8, 8.2, 5.4 Hz, 1H:H_2''''), 3.52 (m, 1H:H_5''), 3.48 (dd, J = 9.7, 1.1 Hz, 1H:H_8'), 3.34 (s, 3H:OCH_3), 3.27 (dt, J = 7.6, 2.4 Hz, 1H:H_3'), 3.04 (dd, J = 9.0, 2.7 Hz, 1H:H_9a), 2.70 (m, 2H:H_4, H_5'), 2.58 (m, 1H:H_4'''), 2.37 (ddd, J = 12.7, 8.4, 5.4 Hz, 1H:H_3'''), 2.05 (dd, J = 13.2, 6.3 Hz, 1H:H_3), 2.01 (m, 1H:H_2'), 1.92 (dd, J = 13.3, 12.0 Hz, 1H:H_3), 1.84 (m, 2H:H_1', H_7'), 1.73 (m, 2H:H_6), 1.61 (m, 1H:H_1'), 1.49 (m, 3H:H_2', H_7', H_3'''), 1.30 (d, J = 7.3 Hz, 3H:H_6), 1.26 (d, J = 7.0 Hz, 3H:H_6'); \textsuperscript{13}C NMR (125 MHz, CDCl_3) δ 180.6 (C_5/C_5'''), 179.5 (C_5/C_5'''), 91.3(C_2), 85.9 (C_8), 79.6 (C_2'''), 69.3 (C_9a), 68.1 (C_3'), 57.4 (OCH_3), 51.8 (C_2), 35.5 (C_3'''), 35.0 (C_4/C_4'''), 34.9 (C_4/C_4'''), 33.9 (C_3), 27.4 (C_6'), 26.83 (C_2/C_7), 26.79 (C_2/C_7), 25.4 (C_4'), 16.4 (C_6), 14.8 (C_6''); HRMS (CI+): calcd for C_{19}H_{30}NO_5: 352.2118 [M+H]^+; found 352.2117.
$^1$H-NMR (CDCl$_3$, 250 MHz)

$^{13}$C-NMR (CDCl$_3$, 62.5 MHz)
$^{1}H$-NMR (CDCl$_3$, 360 MHz)

$^{13}C$-NMR (CDCl$_3$, 90 MHz)
$^{1}$H-NMR (CDCl$_3$, 360 MHz)

$^{13}$C-NMR (CDCl$_3$, 90 MHz)
$^{1}H$-NMR (CDCl$_3$, 250 MHz)

$^{13}$C-NMR (CDCl$_3$, 62.5 MHz)
\[ \begin{align*}
&\text{1H-NMR (CDCl}_3, 360 \text{ MHz))} \\
&\text{13C-NMR (CDCl}_3, 90 \text{ MHz)}
\end{align*} \]
$^{1}$H-NMR (CDCl$_3$, 360 MHz)

$^{13}$C-NMR (CDCl$_3$, 90 MHz)
$^{1}$H-NMR (CDCl$_3$, 360 MHz)

$^{13}$C-NMR (CDCl$_3$, 90 MHz)
$\text{H-NMR (CDCl}_3, 360 \text{ MHz)}$

$\text{C-NMR (CDCl}_3, 90 \text{ MHz)}$
$^1$H-NMR (CDCl$_3$, 360 MHz)

$^{13}$C-NMR (CDCl$_3$, 90 MHz)
$^1$H-NMR (CDCl$_3$, 360 MHz)

$^{13}$C-NMR (CDCl$_3$, 90 MHz)
$^1$H-NMR (CDCl$_3$, 500 MHz)

$^{13}$C-NMR (CDCl$_3$, 125 MHz)
**1H-NMR (CDCl₃, 360 MHz)**

**13C-NMR (CDCl₃, 125 MHz)**
\[ \text{H-NMR (CDCl}_3, 360 \text{ MHz)} \]

\[ \text{C-NMR (CDCl}_3, 125 \text{ MHz)} \]
$\textbf{1H-NMR (CDCl}_3, 500 \text{ MHz)}$
$^1$H-NMR (500 MHz, CDCl$_3$)
epi-2
(alkaloid numbering)

$^{1}$$H$-NMR (CDCl$_3$, 500 MHz)

$^{13}$$C$-NMR (CDCl$_3$, 125 MHz)