Total Synthesis of Hyacinthacine A₁ and 3-*epi*-Hyactinthacine A₁

Laurent Chabaud, Yannick Landais, Philippe Renaud

Supporting Information

General procedure A for acetylation and benzylation of β -hydroxysilanes : To a stirred solution of alcohol in dry CH_2Cl_2 (6.5 mL/mmol) were added acetic anhydride or benzoic anhydride, NEt_3 , and a catalytic amount of 4-DMAP. The resulting mixture was then stirred at RT under nitrogen for 18 h and then was treated with saturated aqueous NaHCO_3 solution. The organic layer was decanted and the aqueous layer extracted with ether. The combined extracts were washed with brine and dried over MgSO_4 , the residue was concentrated in vacuo. The crude product was purified by chromatography through silica gel.

(1R,2S)-2-(dimethyl(phenyl)silyl)-1-((R)-2,2-dimethyl-1,3-dioxolan-4-yl)but-3-enyl acetate

10a.

Prepared according to general procedure A from the corresponding alcohol (9.88 g, 32.3 mmol), Ac_2O (6.1 mL, 64.5 mmol), Et_3N (9.0 mL, 64.5 mmol) and 4-DMAP (390 mg, 3.2 mmol). The crude product was purified by chromatography (Petroleum ether/ EtOAc : 95/5) to afford a colorless oil (10.5 g, 93 %). IR (neat) ν_{max} = 3071-2891 (CH), 1746 (ester), 1626, 1428, 1371, 1279, 1114, 1069 cm^{-1} . ^1H NMR (CDCl_3 , 300 MHz) δ 7.53-7.41 (m, 2H, aromatic H), 7.40-7.29 (m, 3H, aromatic H), 5.84 (ddd, J = 17.1, 10.4, 10.4 Hz, 1H, $\text{CH}=\text{CH}_2$), 5.29 (dd, J = 6.2, 3.0 Hz, 1H, CHOAc), 5.08 (dd, J = 10.4, 1.9 Hz, 1H, $\text{CH}_2=\text{CH}_{\text{cis}}$), 4.98 (ddd, J = 17.1, 1.9, 0.6 Hz, 1H, $\text{CH}_2=\text{CH}_{\text{trans}}$), 4.01 (m, 1H, CHO), 3.75 (m, 1H, CH_2O), 3.68 (m, 1H, CH_2O), 2.16 (dd, J = 10.5, 3.1 Hz, 1H, SiCH), 1.75 (s, 3H, CH_3COO), 1.31 (s, 3H, $\text{C}(\text{CH}_3)_2$), 1.26 (s, 3H, $\text{C}(\text{CH}_3)_2$), 0.35 (s, 3H, SiCH_3), 0.31 (s, 3H, SiCH_3). ^{13}C NMR (CDCl_3 , 75 MHz) δ 169.8 (C_q , $\text{C}=\text{O}$), 136.8 (C_q , aromatic C_q), 134.0 (CH), 133.9 (CH), 129.1 (CH, aromatic CH), 127.6 (CH, aromatic CH), 116.2 (CH_2 , $\text{CH}_2=\text{CH}$), 108.7 (C_q , $\text{C}(\text{CH}_3)_2$), 76.6 (CH, CHOAc), 72.1 (CH, CHO), 65.6 (CH_2 , CH_2O), 37.4 (CH, CHSi), 26.4 (CH_3 , $\text{C}(\text{CH}_3)_2$), 25.3 (CH_3 , $\text{C}(\text{CH}_3)_2$), 20.6 (CH_3 , CH_3COO), -4.2 (CH_3 , SiCH_3), -4.3 (CH_3 , SiCH_3). MS (ESI); m/z (%) : 371 [$\text{M}+\text{Na}$] (100), 329 (21), 231 (10), 209 (10). HRMS [$\text{M}+\text{Na}$] $\text{C}_{19}\text{H}_{28}\text{O}_4\text{SiNa}$: calcd. 372.1654; found. 371.1648. $\text{C}_{19}\text{H}_{28}\text{O}_4\text{Si}$ (348.51): calcd C 65.48, H 8.10; found C 65.73, H 8.02.

(1R,2S)-2-(dimethyl(phenyl)silyl)-1-((R)-2,2-dimethyl-1,3-dioxolan-4-yl)but-3-enyl benzoate

10b.

Prepared according to general procedure A from the corresponding alcohol (842 mg, 2.75 mmol), BzCl (0.64 mL, 5.5 mmol), Et_3N (0.77 mL, 5.5 mmol) and 4-DMAP (33 mg, 0.27 mmol). The crude product was purified by chromatography (Petroleum ether/ EtOAc : 98/2) to afford an inseparable mixture of benzoate and BzCl (351 mg, estimated yield 23%). IR (method) ν_{max} = 3070-2888 (CH), 1789, 1268, 1213, 703 cm^{-1} . ^1H NMR (CDCl_3 , 250 MHz) δ 7.86 (m, 2H, aromatic H), 7.54 (m, 1H, aromatic H), 7.40 (m, 4H, aromatic H), 7.19 (m, 3H, aromatic H), 5.97 (ddd, J = 17.1, 10.4, 10.4 Hz, 1H, $\text{CH}=\text{CH}_2$), 5.55 (dd, J = 6.1, 3.0 Hz, 1H, CHOBz), 5.12 (dd, J = 10.4, 1.4 Hz, 1H, $\text{CH}=\text{CH}_{2\text{cis}}$), 5.02 (dd, J = 17.1, 1.5 Hz, 1H, $\text{CH}=\text{CH}_{2\text{trans}}$), 4.14 (m, 1H, CHO), 3.80 (m, 2H, CH_2O), 2.30 (dd, J = 10.4, 3.0 Hz, 1H, CHSi), 1.27 (s, 3H, $\text{C}(\text{CH}_3)_2$), 1.23 (s, 3H, $\text{C}(\text{CH}_3)_2$), 0.33 (s, 3H, SiCH_3), 0.32 (s, 3H, SiCH_3). ^{13}C NMR (CDCl_3 , 65 MHz) δ 165.4 (C_q , $\text{C}=\text{O}$), 136.6 (C_q , aromatic C_q), 133.9 (CH, aromatic CH), 132.8 (CH, aromatic CH), 130.0 (C_q , aromatic C_q), 129.6 (CH, aromatic CH), 129.0 (CH, aromatic CH), 128.2 (CH, aromatic CH), 127.6 (CH, aromatic CH), 116.5 (CH_2 , $\text{CH}_2=\text{CH}$), 108.9 (C_q , OCO), 76.8 (CH, CHO), 72.8 (CH, CHO), 65.8 (CH_2 , CH_2O), 37.6 (CH, CHSi), 26.4 (CH_3 , $\text{C}(\text{CH}_3)_2$), 25.4 (CH_3 , $\text{C}(\text{CH}_3)_2$), -4.2 (CH_3 , SiCH_3), -4.4 (CH_3 , SiCH_3). MS (ESI); m/z (%) : 433 [$\text{M}+\text{Na}$] (100).

((1R,2S)-1-(methoxymethoxy)-1-((R)-2,2-dimethyl-1,3-dioxolan-4-yl)but-3-en-2-yl)dimethyl(phenyl)silane **10c**.

To a solution of alcohol (400 mg, 1.30 mmol), $\text{EtN}(i\text{-Pr})_2$ (1.08 mL, 6.53 mmol) in CH_2Cl_2 (5.5 mL) at 0°C was added MOMCl (0.5 mL, 6.53 mmol). The solution was stirred for 10 min at this temperature and then for 20h at RT. The mixture was diluted with EtOAc. The organic layer was washed with water, brine and dried over Na_2SO_4 . The crude product was purified

through silica gel (Petroleum ether/EtOAc : 95/5) to afford a colorless oil (393 mg, 86%). IR (neat) ν_{max} = 3071-2823 (CH), 1249, 1114, 1044 cm^{-1} . ^1H NMR (CDCl_3 , 300 MHz) δ 7.56-7.50 (m, 2H, aromatic H), 7.40-7.30 (m, 3H, aromatic H), 5.88 (ddd, J = 17.1, 10.4, 10.4 Hz, 1H, $\text{CH}=\text{CH}_2$), 5.01 (dd, J = 10.2, 1.9 Hz, 1H, $\text{CH}=\text{CH}_2$ *cis*), 4.91 (dd, J = 17.3, 1.5 Hz, 1H, $\text{CH}=\text{CH}_2$ *trans*), 4.60 (d, J = 6.4 Hz, 1H, OCH_2O), 4.53 (d, J = 6.4 Hz, 1H, OCH_2O), 3.98 (m, 1H, CHO), 3.82 (m, 3H, CHO), 3.32 (s, 3H, CH_2OCH_3), 2.08 (dd, J = 10.5, 3.4 Hz, 1H, CHSi), 1.34 (s, 3H, $\text{C}(\text{CH}_3)_2$), 1.24 (s, 3H, $\text{C}(\text{CH}_3)_2$), 0.38 (s, 3H, SiCH_3), 0.30 (s, 3H, SiCH_3). ^{13}C NMR (CDCl_3 , 75 MHz) δ 137.6 (C_q , aromatic C), 135.2 (CH, $\text{CH}=\text{CH}_2$), 133.9 (CH, aromatic CH), 129.2 (CH, aromatic CH), 127.8 (CH, aromatic CH), 115.3 (CH_2 , $\text{CH}_2=\text{CH}$), 108.1 (C_q , $\text{C}(\text{CH}_3)_2$), 97.9 (CH_2 , OCH_2O), 78.7 (CH, CHO), 78.6 (CH, CHO), 65.6 (CH_2 , CH_2O), 56.1 (CH_3 , OCH_3), 39.1 (CH, CHSi), 26.4 (CH_3 , $\text{C}(\text{CH}_3)_2$), 25.0 (CH_3 , $\text{C}(\text{CH}_3)_2$), -3.3 (CH_3 , SiCH_3), -4.7 (CH_3 , SiCH_3). MS (ESI); m/z (%) : 373 [$\text{M}+\text{Na}$] (100). HRMS (LSIMS) [$\text{M}+\text{Na}$] $\text{C}_{19}\text{H}_{30}\text{O}_4\text{SiNa}$: calcd. 373.181108; found. 373.180040.

General procedure B for carboazidation. Di-*tert*-butylhyponitrite (DTBHN) (0.18 eq.) was added every 90 min. to a solution of xanthate (2 eq.), allylsilane (1 eq.), arylsulfonylazide (3 eq.) and $(\text{Bu}_3\text{Sn})_2$ (1.5 eq.) in dry degassed benzene (2 mL/mmol of xanthate) at reflux (80 or 60°C) under N_2 . The reaction was monitored by TLC. Upon completion, the solvent was removed under reduced pressure and the crude product purified through silica gel (pentane, then pentane/EtOAc).

6-Acetoxy-4-azido-6-(2,2-dimethyl-[1,3]dioxolan-4-yl)-5-(dimethyl-phenyl-silanyl)-hexanoic acid ethyl ester **11a**.

Prepared according to general procedure B from allylsilane **10a** (244 mg, 0.7 mmol), xanthate (71 mg, 0.34 mmol), 3-pyridinesulfonyl azide (194 mg, 1.05 mmol), $(\text{Bu}_3\text{Sn})_2$ (0.26 mL, 0.52 mmol), DTBHN (11 mg, 0.06 mmol) in benzene (1 mL) at 60°C under N_2 atmosphere. The product was obtained as a colorless oil (137 mg, 84%, *syn/anti* 82/18) after

purification through silica gel (pentane then pentane/EtOAc : 95/5). Major diastereomer: **10a syn** : $[\alpha_D]^{20} = +74.7^\circ$ ($C = 1.08$, CHCl_3). IR (neat) ν_{max} = 3070-2984 (CH), 2105 (CHN_3), 1732 (ester) cm^{-1} . ^1H NMR (CDCl_3 , 300 MHz) δ 7.58-7.51 (m, 2H, aromatic H), 7.38-7.32 (m, 3H, aromatic H), 5.09 (dd, J = 6.9, 1.6 Hz, 1H, CHOAc), 4.14 (q, J = 7.2 Hz, 2H, $\text{CH}_3\text{CH}_2\text{O}$), 4.10-3.97 (m, 2H, CHO, CHN_3), 3.81 (dd, J = 8.6, 6.3 Hz, 1H, CH_2O), 3.54 (dd, J = 8.6, 6.1 Hz, 1H, CH_2O), 2.42 (m, 2H, CH_2COO), 1.96 (s, 3H, CH_3COO), 1.81 (m, 2H, $\text{CH}_2\text{CH}_2\text{CO}$), 1.69 (m, 1H, CHSi), 1.27 (t, J = 7.2 Hz, 3H, $\text{CH}_3\text{CH}_2\text{O}$), 1.27 (s, 3H, $\text{C}(\text{CH}_3)_2$), 1.23 (s, 3H, $\text{C}(\text{CH}_3)_2$), 0.42 (s, 6H, $\text{Si}(\text{CH}_3)_2$). ^{13}C NMR (CDCl_3 , 75 MHz) δ 172.8 (C_q , CH_2OCO), 170.4 (C_q , CH_3COO), 137.4 (C_q , aromatic C_q), 134.2 (CH, aromatic CH), 129.2 (CH, aromatic CH), 127.8 (CH, aromatic CH), 109.4 (C_q , OCO), 75.8 (CH, CHOAc), 72.4 (CH, CHO), 66.8 (CH_2 , CH_2O), 62.9 (CH, CHN_3), 60.4 (CH_2 , $\text{CH}_3\text{CH}_2\text{O}$), 35.0 (CH, CHSi), 32.2 (CH_2), 31.6 (CH_2), 26.3 (CH_3 , $\text{C}(\text{CH}_3)_2$), 25.2 (CH_3 , $\text{C}(\text{CH}_3)_2$), 21.6 (CH_3 , CH_3COO),

14.2 (CH₃, CH₃CH₂O), -2.0 (CH₃, SiCH₃), -3.2 (CH₃, SiCH₃). MS (ESI); m/z (%) : 500 (100) [M+Na], 435 (21) [M-N₃], 418 (20), 329 (28), 317 (53), 223 (54). HRMS [M+Na] C₂₃H₃₅N₃O₆SiNa: calcd. 500.2192, found. 500.2177. C₂₈H₃₇N₃O₆Si (539.7): calcd C 57.84, H 7.39, Si 5.88; found C 57.89, H 7.51, Si 5.86. Minor diastereomer: **10a anti** : IR (neat) $\nu_{\max}$ = 3070-2984 (CH), 2105 (CHN₃), 1732 (ester) cm⁻¹. ¹H NMR (CDCl₃, 300 MHz) δ 7.56-7.47 (m, 2H, aromatic H), 7.41-7.32 (m, 3H, aromatic H), 5.24 (dd, J = 7.3, 4.0 Hz, 1H, CHOAc), 4.21 (m, 1H, CHO), 4.13 (q, J = 7.1 Hz, 2H, CH₃CH₂O), 3.82 (m, 1H, CHN₃), 3.73-3.60 (m, 2H, CH₂O), 2.38 (m, 2H, CH₂COO), 2.11-2.02 (m, 1H, CH₂CH₂CO), 2.01 (s, 3H, CH₃O), 1.81 (m, 1H, CHSi), 1.77-1.66 (m, 1H, CH₂CH₂CO), 1.31-1.21 (m, 9H, CH₃CH₂O, C(CH₃)₂), 0.44 (s, 6H, Si(CH₃)₂). ¹³C NMR (CDCl₃, 75 MHz) δ 172.7 (C_q, CH₂OCO), 170.0 (C_q, CH₃COO), 137.7 (C_q, aromatic C_q), 134.7 (CH, aromatic CH), 129.3 (CH, aromatic CH), 128.0 (CH, aromatic CH), 109.3 (C_q, OCO), 76.2 (CH, CHO), 73.1 (CH, CHOAc), 67.0 (CH₂, CH₂O), 62.2 (CH, CHN₃), 60.4 (CH₂, CH₃CH₂O), 33.2 (CH, CHSi), 31.5 (CH₂), 30.3 (CH₂), 26.4 (CH₃, C(CH₃)₂), 25.2 (CH₃, C(CH₃)₂), 21.1 (CH₃, CH₃COO), 14.2 (CH₃, CH₃CH₂O), -2.3 (CH₃, SiCH₃), -2.4 (CH₃, SiCH₃). MS (LSIMS); m/z (%) : 500 (100) [M+Na], 435 (21) [M-N₃], 393 (17), 305 (40), 241 (52). HRMS [M+Na] C₂₃H₃₅N₃O₆SiNa: calcd. 500.219284, found. 500.217543.

(1R,2S)-3-azido-2-(dimethyl(phenyl)silyl)-1-(2,2-dimethyl-1,3-dioxolan-4-yl)-6-ethoxy-6-oxohexyl benzoate **11b**.

Prepared according to general procedure B from allylsilane **10b** (containing BzCl) (261 mg, 0.63 mmol), xanthate (70 mg, 0.34 mmol), 3-pyridinesulfonyl azide (187 mg, 1.02 mmol), (Bu₃Sn)₂ (0.47 mL, 0.24 mmol), DTBHN (10 mg, 0.06 mmol) in benzene at 60°C under N₂ atmosphere. The product was obtained as a colorless oil (77 mg, estimated yield 30%, *syn/anti* 80/20) after

purification through silica gel (pentane then pentane/EtOAc : 9/1). IR (method) $\nu_{\max}$ = 3070-2854 (CH), 2101 (CHN₃), 1790, 1724 (ester), 1264, 1110 cm⁻¹. ¹H NMR (CDCl₃, 300MHz) δ 8.01 (m, 2H *maj* + 2H *min*, aromatic H), 7.54 (m, 5H *maj* + 5H *min*, aromatic H), 7.44 (m, 2H *maj* + 2H *min*, aromatic H), 7.32 (m, 1H *maj* + 1H *min*, aromatic H), 5.53 (dd, J = 7.2, 4.5 Hz, 1H, CHOBz *min*), 5.45 (dd, J = 7.3, 3.2 Hz, 1H, CHOBz *maj*), 4.35 (m, 1H, CHO *min*), 4.24 (m, 1H, CHO *maj*), 4.14 (q, J = 7.1 Hz, 2H, CH₂O *maj*), 4.13-4.09 (m, 2H *min* CH₂O + 1H *maj* CHN₃), 3.96 (m, 1H, CHN₃ *min*), 3.79-3.65 (m, 2H *maj* + 2H *min*, CH₂O), 2.56-2.33 (m, 2H *maj* + 2H *min*, CH₂CO), 2.01-1.86 (m, 2H *maj* + 2H *min*, CH₂CHN₃), 1.81 (m, 1H *maj* + 1H *min*, CHSi), 1.30-1.22 (m, 6H *maj* CH₃CH₂, CH₃ + 9H *min* CH₃CH₂O, C(CH₃)₂), 1.20 (s, 3H, CH₃ *maj*), 0.46 (s, 3H, CH₃Si *min*), 0.45 (s, 3H, CH₃Si *min*), 0.44 (s, 3H, CH₃Si *maj*), 0.42 (s, 3H, CH₃Si *maj*). **Major diastereomer** : ¹³C NMR (CDCl₃, 75 MHz) δ 172.8 (C_q, C=O), 165.9 (C_q, C=O), 137.7 (C_q, aromatic C), 134.0 (CH, aromatic CH), 133.7 (CH, aromatic CH), 133.2 (CH, aromatic CH), 129.8 (C_q, aromatic C), 129.2 (CH, aromatic CH), 128.4 (CH, aromatic CH), 127.9 (CH, aromatic CH), 109.4 (C_q, OCO), 75.8 (CH, CHOBz), 73.6 (CH, CHO), 66.7 (CH₂, CH₂O), 62.5 (CH, CHN₃), 60.5 (CH₂, CH₃CH₂O), 34.5 (CH, CHSi), 31.6 (CH₂), 31.5 (CH₂), 26.3 (CH₃, C(CH₃)₂), 25.2 (CH₃, C(CH₃)₂), 14.2 (CH₃, CH₃CH₂O), -1.7 (CH₃, SiCH₃), -3.0 (CH₃, SiCH₃). MS (LSIMS); m/z (%) : 562 [M+Na] (59), 497 [M-N₃] (11). HRMS [M+Na] C₂₈H₃₇N₃O₆SiNa: calcd. 562.234934; found. 562.235301.

(4S,5R,6S)-ethyl 4-azido-6-(methoxymethoxy)-5-(dimethyl(phenyl)silyl)-6-((R)-2,2-dimethyl-1,3-dioxolan-4-yl)hexanoate **11c**.

Prepared according to general procedure B from allylsilane **10c** (393 mg, 1.12 mmol), xanthate (124 mg, 0.60 mmol), 3-pyridinesulfonyl azide (309 mg, 1.68 mmol), $(Bu_3Sn)_2$ (0.42 mL, 0.84 mmol), DTBHN (18 mg, 0.1 mmol) in benzene (2 mL) at 60°C under N_2 atmosphere. The residue was purified through silica gel (pentane then pentane/EtOAc: 95/5) to afford an inseparable mixture of two diastereomers (*syn/anti* : 61/39)

as a colorless oil (149 mg, 52%). IR (neat) ν_{max} = 3070-2825 (CH), 2105 (CHN_3), 1732 (ester), 1371, 1258, 1111, 819 cm^{-1} . 1H NMR ($CDCl_3$, 300 MHz) δ 7.56-7.49 (m, 2H *maj* + 2H *min*, aromatic H), 7.39-7.32 (m, 3H *maj* + 3H *min*, aromatic H), 4.63 (d, J = 6.8 Hz, 1H, OCH_2O *maj*), 4.62 (d, J = 6.8 Hz, 1H, OCH_2O *min*), 4.56 (d, J = 6.4 Hz, 1H, OCH_2O *min*), 4.53 (d, J = 6.8 Hz, 1H, OCH_2O *maj*), 4.23-4.01 (m, 2H *maj* + 2H *min*, CH_2OCO , 1H *maj*, CHN_3 , 1H *maj* + 1H *min*, CHO), 3.91 (m, 1H, CHN_3 *min*), 3.82 (m, 2H *min*, CHO, $CHOMOM$), 3.74 (dd, J = 8.6, 6.2 Hz, 1H *maj*, CHO), 3.70 (m, 1H *min*, CHO), 3.62 (dd, J = 6.0, 3.0 Hz, 1H, CHO *maj*), 3.56 (dd, J = 8.3, 6.8 Hz, 1H, CHO *maj*), 3.35 (s, 3H, OCH_3 *min*), 3.33 (s, 3H, OCH_3 *maj*), 2.53-2.31 (m, 2H *maj* + 2H *min*, CH_2CO), 2.07 (m, 1H, CH_2CH_2CO *min*), 1.83 (m, 2H, CH_2CH_2CO *maj*), 1.75 (dd, J = 7.3, 4.3 Hz, 1H, $CHSi$ *min*), 1.62 (m, 1H, CH_2CH_2CO *min*), 1.59 (m, 1H, $CHSi$ *maj*), 1.34 (s, 3H, CH_3 *min*), 1.30-1.21 (m, 9H OCH_2CH_3 *maj*, $C(CH_3)_2$ *maj* + 6H OCH_2CH_3 *min*, CH_3 *min*), 0.47 (s, 3H *maj* + 3H *min*, $SiCH_3$), 0.44 (s, 3H, $SiCH_3$ *min*), 0.43 (s, 3H, $SiCH_3$ *maj*). ^{13}C NMR ($CDCl_3$, 63 MHz) δ 173.0 (C_q , C=O *maj*), 172.9 (C_q , C=O *min*), 138.7 (C_q , aromatic C *min*), 138.4 (C_q , aromatic C *maj*), 133.9 (CH, aromatic CH *maj*), 133.6 (CH, aromatic CH *min*), 129.2 (CH, aromatic CH *min*), 129.1 (CH, aromatic CH *maj*), 128.0 (CH, aromatic CH *min*), 127.9 (CH, aromatic CH *maj*), 108.9 (C_q , OCO *min*), 108.8 (C_q , OCO *maj*), 97.7 (CH_2 , OCH_2O *maj*), 97.6 (CH_2 , OCH_2O *min*), 80.2 (CH, CHO *min*), 79.9 (CH, CHO *maj*), 77.6 (CH, $CHOMOM$ *min*), 77.1 (CH, $CHOMOM$ *maj*), 67.7 (CH_2 , CH_2O *min*), 66.9 (CH_2 , CH_2O *maj*), 62.7 (CH, CHN_3), 62.6 (CH, CHN_3), 60.4 (CH_2 , CH_2OCO *maj* + *min*), 56.1 (CH_3 , OCH_3 *min*), 55.9 (CH_3 , OCH_3 *maj*), 36.3 (CH, $CHSi$ *maj*), 34.8 (CH, $CHSi$ *min*), 31.9 ($2^{\circ}CH_2$ *maj*), 31.6 (CH_2 , *min*), 30.0 (CH_2 , *min*), 26.4 (CH_3 , $C(CH_3)_2$ *min*), 26.3 (CH_3 , $C(CH_3)_2$ *maj*), 25.1 (CH_3 , $C(CH_3)_2$ *min*), 24.9 (CH_3 , $C(CH_3)_2$ *maj*), 14.2 ($2^{\circ}CH_3$, CH_3CH_2O *maj* + *min*), -1.0 (CH_3 , $SiCH_3$ *maj*), -1.6 (CH_3 , $SiCH_3$ *min*), -1.9 (CH_3 , $SiCH_3$ *min*), -3.0 (CH_3 , $SiCH_3$ *maj*). MS (LSIMS) m/z (%): 502 [$M+Na$] (100), 437 (47), 288 (42), 241 (66). HRMS [$M+Na$] $C_{23}H_{37}N_3O_6SiNa$: calcd. 502.234934, found. 502.235986.

(1S,2R)-2-(dimethyl(phenyl)silyl)-1-((R)-2,2-dimethyl-1,3-dioxolan-4-yl)but-3-enyl acetate

12.

Prepared according to general procedure A from the corresponding alcohol (2.4 g, 7.84 mmol), Ac_2O (1.48 mL, 15.7 mmol), Et_3N (2.2 mL, 15.7 mmol) and 4-DMAP (95 mg, 0.8 mmol). The crude mixture was purified by chromatography (Petroleum ether/EtOAc : 95/5) to afford a colorless oil (2.46 g, 90 %).

IR (neat) ν_{max} = 3071-2899 (CH), 1746 (ester), 1370, 1234, 1073 cm^{-1} . 1H NMR ($CDCl_3$, 300 MHz) δ 7.49-7.43 (m, 2H, aromatic H), 7.38-7.31 (m, 3H, aromatic H), 5.88 (ddd, J = 17.1, 10.4, 10.4 Hz, 1H, $CH=CH_2$), 5.17 (dd, J = 7.2, 3.8 Hz, 1H, $CHOAc$), 5.02 (dd, J = 10.2, 1.9 Hz, 1H, $CH_2=CH_{cis}$), 4.84 (dd, J = 17.1, 1.3 Hz, 1H, $CH_2=CH_{trans}$), 4.12 (ddd, J = 13.9, 6.8, 6.8 Hz, 1H, CHO), 3.93 (dd, J = 8.3, 6.4 Hz, 1H, CH_2O), 3.57 (dd, J = 8.3, 6.4 Hz, 1H, CH_2O), 1.92 (dd, J = 10.5, 3.8 Hz, 1H, $CHSi$), 1.82 (s, 3H, CH_3COO), 1.36 (s, 3H, $C(CH_3)_2$), 1.25 (s, 3H, $C(CH_3)_2$), 0.36 (s, 3H, $SiCH_3$), 0.31 (s, 3H,

SiCH₃). ¹³C NMR (CDCl₃, 75 MHz) δ 170.0 (C_q, C=O), 136.8 (C_q, aromatic C), 134.2 (CH), 134.1 (CH), 129.2 (CH, aromatic CH), 127.7 (CH, aromatic CH), 115.6 (C_q, OCO), 109.7 (CH₂, CH₂=CH), 77.1 (CH, CHO), 73.0 (CH, CHOAc), 65.7 (CH₂, CH₂O), 38.0 (CH, CHSi), 26.2 (CH₃, C(CH₃)₂), 25.6 (CH₃, C(CH₃)₂), 20.9 (CH₃, CH₃COO), -3.8 (CH₃, SiCH₃), -4.2 (CH₃, SiCH₃). MS (LSIMS); *m/z* (%): 371 (36) [M+Na], 289 (34). HRMS [M+Na] C₁₉H₂₈O₄SiNa: calcd. 371.165458; found. 371.165985. C₁₉H₂₈O₄Si (348.51): calcd C 65.48, H 8.10; found C 65.80, H 8.11.

(5R,6S)-ethyl 6-acetoxy-4-azido-5-(dimethyl(phenyl)silyl)-6-((R)-2,2-dimethyl-1,3-dioxolan-4-yl)hexanoate **13**.

Prepared according to general procedure B from allylsilane **12** (703 mg, 2.02 mmol), xanthate (207 mg, 1.0 mmol), 3-pyridinesulfonyl azide (1.84 g, 10 mmol), (Bu₃Sn)₂ (0.76 mL, 1.5 mmol), DTBHN (32 mg, 0.18 mmol) in benzene (2 mL) at 60°C under N₂ atmosphere. The residue was purified through silica gel (pentane then pentane/EtOAc : 9/1) to obtain the product as a colorless oil (269 mg, 57%, *syn/anti* 80/20).

Major diastereomer : IR (neat) $\nu_{\max}$ = 3071-2984 (CH), 2104 (CHN₃), 1732 (ester) cm⁻¹. ¹H NMR (CDCl₃, 250 MHz) δ 7.60-7.48 (m, 2H, aromatic H), 7.42-7.30 (m, 3H, aromatic H), 5.19 (dd, *J* = 5.8, 2.1 Hz, 1H, CHOAc), 4.19-4.01 (m, 4H, CH₃CH₂O, CHO, CHN₃), 3.89 (dd, *J* = 8.5, 6.4 Hz, 1H, CH₂O), 3.4 (dd, *J* = 8.7, 5.9 Hz, 1H, CH₂O), 2.50-2.25 (m, 2H, CH₂CO), 2.06 (s, 3H, CH₃COO), 1.79-1.67 (m, 2H, CH₂CHN₃), 1.60 (m, 1H, CHSi), 1.33 (s, 3H, CH₃), 1.30-1.21 (m, 6H, CH₃CH₂O, CH₃), 0.43 (s, 3H, Si(CH₃)₂), 0.42 (s, 3H, Si(CH₃)₂). ¹³C NMR (CDCl₃, 63 MHz) δ 172.8 (C_q, CH₂OCO), 170.4 (C_q, CH₃COO), 137.2 (C_q, aromatic C_q), 134.2 (CH, aromatic CH), 129.3 (CH, aromatic CH), 127.9 (CH, aromatic CH), 109.9 (C_q, OCO), 78.1 (CH, CHOAc), 71.2 (CH, CHO), 66.1 (CH₂, CH₂O), 62.8 (CH, CHN₃), 60.5 (CH₂, CH₂OCO), 37.3 (CH, CHSi), 32.1 (CH₂), 31.7 (CH₂), 25.9 (CH₃, C(CH₃)₂), 25.4 (CH₃, C(CH₃)₂), 21.6 (CH₃, CH₃COO), 14.2 (CH₃, CH₃CH₂O), -2.2 (CH₃, SiCH₃), -3.2 (CH₃, SiCH₃). MS (LSIMS) *m/z* (%) : 500 (100) [M+Na], 435 (16), 288 (35). HRMS [M+Na] C₂₃H₃₅N₃O₆SiNa: calcd. 500.219284, found. 500.218781. C₂₈H₃₇N₃O₆Si (539.7): calcd C 57.84, H 7.39; found C 57.88, H 7.36.

(5R,6S)-ethyl-6-acetoxy-6-((4S)-5-azido-2,2-dimethyl-1,3-dioxolan-4-yl)-5-

(dimethyl(phenyl)silyl)hexanoate **14**.

Prepared according to general procedure B from allylsilane **12** (375 mg, 1.08 mmol), xanthate (447 mg, 2.15 mmol), 3-Pyridinesulfonyl azide (600 mg, 3.25 mmol), (Bu₃Sn)₂ (0.82 mL, 1.62 mmol), DTBHN (32 mg, 0.18 mmol) in benzene (4.3 mL) at 60°C under N₂ atmosphere. The residue was purified through silica gel (pentane then pentane/EtOAc: 95/5) to

obtain a colorless oil (209 mg, 41%). IR (neat) $\nu_{\max}$ = 3070-2900 (CH), 2107 (CHN₃), 1732 (ester), 1236, 1111 cm⁻¹. ¹H NMR (CDCl₃, 300 MHz) δ 7.56-7.44 (m, 2H, aromatic H), 7.41-7.31 (m, 3H, aromatic H), 5.18 (dd, *J* = 6.4, 4.1 Hz, 1H, CHOAc), 5.10 (d, *J* = 4.1 Hz, 1H, OCHN₃), 4.10 (q, *J* = 7.1 Hz, 2H, CH₂OCO), 3.89 (m, 1H, CHO), 2.29-2.11 (m, 2H, CH₂CO), 2.00 (s, 3H, CH₃COO), 1.72-1.46 (m, 4H, CH₂CH₂), 1.43 (s, 3H, CH₃), 1.32 (s, 3H, CH₃), 1.29 (m, 1H, CHSi), 1.23 (t, *J* = 7.1 Hz, 3H, CH₃CH₂O), 0.37 (s, 3H, SiCH₃), 0.35 (s, 3H, SiCH₃). ¹³C NMR (CDCl₃, 75 MHz) δ 173.2 (C_q, C=O), 170.6 (C_q, C=O), 137.8 (C_q, aromatic C), 133.8 (CH, aromatic CH), 129.2 (CH, aromatic CH), 127.8 (CH, aromatic CH), 112.4 (C_q, OCO), 90.8 (CH, OCHN₃), 82.6 (CH, CHO), 72.3 (CH, CHOAc), 60.2 (CH₂, CH₂OCO), 34.4 (CH₂, CH₂CO), 28.1 (CH, CHSi), 26.8 (CH₃, C(CH₃)₂), 26.0 (CH₃, C(CH₃)₂),

25.9 (CH₂), 25.3 (CH₂), 20.9 (CH₃, CH₃COO), 14.2 (CH₃, CH₃CH₂O), -3.2 (CH₃, SiCH₃), -3.6 (CH₃, SiCH₃). MS (ESI) m/z (%) : 500 (100) [M+Na]. HRMS [M+Na] C₂₃H₃₅N₃O₆SiNa: calcd. 500.2193, found. 500.2174.

(4R,5S,6S)-ethyl 6-acetoxy-4-azido-5-hydroxy-6-((R)-2,2-dimethyl-1,3-dioxolan-4-yl)hexanoate **15a, 15b**.

Peracetic acid (36–40% in AcOH, 4.88 mL, 28.7 mmol) was added dropwise to a stirred mixture of *syn*-silane **10a** (2.7 g, 5.66 mmol), potassium bromide (1.2 g, 10.1 mmol) and sodium acetate (1.35 g, 16.4 mmol) in acetic acid (29 mL) at 0°C. The mixture was allowed to warm to room temperature and more peracetic acid (17 mL, 100.2 mmol) and sodium acetate (4.7 g, 57.1 mmol) were added and the mixture stirred

overnight. The mixture was quenched with aqueous sodium thiosulfate solution (25%) at 0°C and the aqueous layer saturated with salt. The mixture was extracted with ethyl acetate. The combined organic layers were washed with saturated aqueous sodium hydrogen carbonate and brine, dried (Na₂SO₄) and concentrated under reduced pressure. The residue was chromatographed (SiO₂, Pentane/EtOAc : 8/2) to give a 76/24 mixture of the alcohol (1.72 g, 85%) corresponding to acyl migration.

In order to allow an easier characterization of the products, the crude mixture of alcohol was acetylated, according to general procedure A, from alcohol (40 mg, 0.11 mmol), Ac₂O (0.02 mL, 0.22 mmol), NEt₃ (0.03 mL, 0.22 mmol) and 4-DMAP (1.2 mg, 0.01 mmol). The crude product was purified by chromatography through silica (Petroleum Ether/EtOAc: 8/2) to afford the corresponding diacetate as a colorless oil (34.2 mg, 77% over two steps).

IR (neat) $\nu_{\max}$ = 2986-2938 (CH), 2105 (CHN₃), 1748 (ester) cm⁻¹. ¹H NMR (CDCl₃, 400 MHz) δ 5.22 (dd, J = 5.6, 4.1 Hz, 1H, CHOAc), 5.14 (dd, J = 6.7, 4.2 Hz, 1H, CHOAc), 4.32 (q, J = 6.5 Hz, 1H, CHO), 4.14 (q, J = 7.1 Hz, 2H, CH₃CH₂O), 4.07 (dd, J = 8.6, 6.4 Hz, 1H, CH₂O), 3.80 (dd, J = 8.6, 6.1 Hz, 1H, CH₂O), 3.69 (m, 1H, CHN₃), 2.48 (m, 2H, CH₂COO), 2.14 (s, 3H, CH₃), 2.07 (s, 3H, CH₃), 1.99 (m, 1H, CH₂CHN₃), 1.85 (m, 1H, CH₂CHN₃), 1.41 (s, 3H, C(CH₃)₂), 1.36 (s, 3H, C(CH₃)₂), 1.27 (t, J = 7.2 Hz, 3H, CH₃CH₂O). ¹³C NMR (CDCl₃, 126 MHz) δ 172.4 (C_q, CH₂OCO), 169.8 (C_q, CH₃COO), 169.7 (C_q, CH₃COO), 110.0 (C_q, OCO), 73.7 (CH, CHOAc), 73.4 (CH, CHO), 71.6 (CH, CHOAc), 66.5 (CH₂, OCHCH₂O), 60.6 (CH₂, CH₃CH₂O), 60.5 (CH, CHN₃), 30.4 (CH₂, CH₂CO), 26.2 (CH₃, C(CH₃)₂), 26.1 (CH₂, CH₂CH₂CO), 25.2 (CH₃, C(CH₃)₂), 20.7 (CH₃, CH₃COO), 20.6 (CH₃, CH₃COO), 14.2 (CH₃, CH₃CH₂O). MS (ESI); m/z (%) : 424 [M+Na] (38), 402 (7), 344 (100), 196 (29). HRMS [M+Na] C₁₇H₂₇N₃O₈Na: calcd. 424.1695, found. 424.1703.

(R)-methyl 4-azido-4-((4S,5R)-5-((R)-1,2-dihydroxyethyl)-2,2-dimethyl-1,3-dioxolan-4-yl)butanoate **16**.

To a stirred solution of **15a/15b** (87 mg, 0.23 mmol) in MeOH (2 mL) was added DOWEX 1X10 (CO₃²⁻ form) (174 mg). The resulting mixture was stirred overnight at RT. The resin was filtered off and the solvent evaporated under vacuum. The crude diol was dissolved in a mixture of CH₂Cl₂ (1 mL) and 2,2-dimethoxypropane (1 mL), and a catalytic amount of *p*-TsOH was added. The solution was stirred overnight at RT, then the

mixture was washed with aqueous saturated NaHCO_3 . The aqueous layer was extracted with Et_2O and the combined organic layer washed with brine. The solvent was evaporated under vacuum. The crude diacetone was dissolved in CH_3CN (1.2 mL) and $\text{Zn}(\text{NO}_3)_2 \cdot 6\text{H}_2\text{O}$ (342 mg, 1.15 mmol) was added. The resulting mixture was stirred at 50°C for 6h. The solvent was evaporated and the oily residue dissolved in CH_2Cl_2 , washed with brine and dried over Na_2SO_4 . The solvent was evaporated under vacuo and the residue purified through silica gel (Petroleum ether/ EtOAc : 5/5) to afford a colorless oil (39 mg, 56%, corrected yield 75%). IR (neat) ν_{max} = 3428 (OH), 2990-2930 (CH), 2106 (CHN_3), 1732 (ester) cm^{-1} . ^1H NMR (CDCl_3 , 300 MHz) δ 4.20 (m, 1H, CHO), 4.10-3.95 (m, 2H, CHO), 3.92-3.81 (br, 1H, CHO), 3.70 (s, 3H, OCH_3), 3.69-3.57 (m, 2H, CHO, CHN_3), 3.17 (br, 1H, OH), 2.55 (dd, J = 7.6, 6.4 Hz, 2H, CH_2CO), 2.23-2.02 (m, 2H, CH_2CHN_3 , OH), 1.99-1.82 (m, 1H, CH_2CHN_3), 1.48 (s, 3H, $\text{C}(\text{CH}_3)_2$), 1.36 (s, 3H, $\text{C}(\text{CH}_3)_2$). ^{13}C NMR (CDCl_3 , 75 MHz) δ 173.8 (C_q , $\text{C}=\text{O}$), 108.9 (C_q , OCO), 80.0 (CH, CHO), 77.0 (CH, CHO), 69.2 (CH, CHO), 64.6 (CH_2 , CH_2OH), 58.7 (CH, CHN_3), 51.9 (CH_3 , CH_3OCO), 30.4 (CH_2 , CH_2COO), 27.2 (CH_3 , $\text{C}(\text{CH}_3)_2$), 26.8 (CH_2 , CH_2CHN_3), 25.0 (CH_3 , $\text{C}(\text{CH}_3)_2$). MS (LSIMS); m/z (%) : 326 (58) $[\text{M}+\text{Na}]$. HRMS $[\text{M}+\text{Na}]$ $\text{C}_{12}\text{H}_{21}\text{N}_3\text{O}_6\text{Na}$: calcd. 326.132805; found. 326.133367.

Methyl 4-azido-4-(5-{2- $\{[tert\text{-butyl(dimethyl)silyl]oxy\}-1-[(methylsulfonyl)oxy]ethyl\}-2,2\text{-dimethyl-1,3-dioxolan-4-yl}butanoate$ **17**.

To a solution of diol **16** (114 mg, 0.38 mmol) in pyridine (5.6 mL) was added TBDMSCl (170 mg, 1.13 mmol). The mixture was stirred at RT for 5h under N_2 atmosphere. The solution was washed with brine then with CuSO_4 saturated solution to removed pyridine. The solvent was evaporated under vacuo. To a solution of the crude alcohol in pyridine (6 mL) was added MsCl (0.29 mL, 3.79 mmol) and the reaction was stirred for 3h at RT. The reaction was quenched with

brine and the aqueous layer extracted with CH_2Cl_2 . The organic layer was washed with brine then dried over Na_2SO_4 . The residue was purified through silica (Petroleum ether/ EtOAc : 9/1) to afford a colorless oil (157 mg, 84% over two steps). IR (neat) ν_{max} = 2954-2857 (CH), 2107 (CHN_3), 1737 (ester), 1361, 1258, 1177, 921, 837 cm^{-1} . ^1H NMR (CDCl_3 , 250 MHz) δ 5.04 (m, 1H, CHOMs), 4.41 (dd, J = 7.0, 7.0 Hz, 1H, CHO), 4.21 (dd, J = 6.7, 4.0 Hz, 1H, CHO), 4.09 (dd, J = 12.2, 2.1 Hz, 1H, CHO), 3.91 (dd, J = 12.2, 4.9 Hz, 1H, CHO), 3.69 (s, 3H, CH_3OCO), 3.51 (m, 1H, CHN_3), 3.12 (s, 3H, SO_2CH_3), 2.55 (dd, J = 7.3, 7.3 Hz, 2H, CH_2COO), 2.12-1.96 (m, 2H, CH_2CHN_3), 1.51 (s, 3H, $\text{C}(\text{CH}_3)_2$), 1.35 (s, 3H, $\text{C}(\text{CH}_3)_2$), 0.91 (s, 9H, $\text{SiC}(\text{CH}_3)_3$), 0.1 (s, 3H, SiCH_3), 0.09 (s, 3H, SiCH_3). ^{13}C NMR (CDCl_3 , 63.5 MHz) δ 173.1 (C_q , $\text{C}=\text{O}$), 109.1 (C_q , OCO), 81.2 (CH, CHO), 78.9 (CH, CHO), 74.3 (CH, CHO), 62.3 (CH_2 , CH_2OTBS), 58.2 (CH, CHN_3), 51.8 (CH_3 , CH_3OCO), 39.2 (CH_3 , OSO_2CH_3), 30.3 (CH_2 , CH_2COO), 26.6 (CH_2 , CH_2CHN_3), 26.3 (CH_3 , $\text{SiC}(\text{CH}_3)_3$), 25.8 (CH_3 , $\text{C}(\text{CH}_3)_2$), 24.4 (CH_3 , $\text{C}(\text{CH}_3)_2$), 18.3 (C_q , $\text{SiC}(\text{CH}_3)_3$), -5.5 (CH_3 , SiCH_3), -5.6 (CH_3 , SiCH_3). MS (LSMIS); m/z (%) : 518 (100) $[\text{M}+\text{Na}]$, 468 (70), 410 (26). HRMS $[\text{M}+\text{Na}]$ $\text{C}_{19}\text{H}_{37}\text{N}_3\text{O}_8\text{SSiNa}$: calcd. 518.196836; found 518.196731.

Methyl 3-((3aS,4R,6S,6aR)-6-((tert-butyl dimethylsilyloxy)methyl)-2,2-dimethyl-tetrahydro-3aH-[1,3]dioxolo[4,5-c]pyrrol-4-yl)propanoate **18**.

Indium powder (20 mg, 0.176 mmol) and NH_4Cl (9.5 mg, 0.176 mmol) were added to a solution of the azide **17** (43.5 mg, 0.088 mmol) in dry methanol (0.5 mL). The reaction mixture was stirred under reflux for 3 h. Then Et_3N (0.06 mL, 0.44 mmol) was added, and the reaction mixture was stirred

under reflux for 3 h. The cooled reaction mixture was diluted with EtOAc, stirred for 10 min, and filtered through a short pad of celite. The solvent was removed under reduced pressure, and the crude product was purified by flash chromatography (CH₂Cl₂/MeOH: 99/1) to afford a yellow oil (33 mg, 100%). IR (neat) $\nu_{\max}$ = 2931-2857 (CH), 1738 (ester) cm⁻¹. ¹H NMR (CDCl₃, 300 MHz) δ 4.59 (dd, J = 5.8, 4.0 Hz, 1H, CH_eO), 4.51 (dd, J = 5.8, 4.0 Hz, 1H, CH_fO), 3.67 (s, 3H, CH₃OCO), 2.86 (ddd, J = 6.4, 6.4, 3.8 Hz, 1H, CH_gN), 2.75 (ddd, J = 7.2, 7.2, 4.0 Hz, 1H, CH_dN), 2.47 (dd, J = 7.5, 1.7 Hz, 2H, CH₂CO), 1.93 (m, 2H, CH_{2c}), 1.84 (br, 1H, NH), 1.43 (s, 3H, C(CH₃)₂), 1.29 (s, 3H, C(CH₃)₂), 0.89 (s, 9H, SiC(CH₃)₃), 0.06 (s, 6H, Si(CH₃)₂). ¹³C NMR (CDCl₃, 75 MHz) δ 173.9 (C_q, C=O), 110.8 (C_q, OCO), 81.4 (CH, CHO), 81.0 (CH, CHO), 63.9 (CH, CHN), 61.7 (CH, CHN), 61.5 (CH₂, CH₂OSi), 51.6 (CH₃, CH₃OCO), 31.6 (CH₂, CH₂CO), 26.0 (CH₃, SiC(CH₃)₃), 25.7 (CH₃, C(CH₃)₂), 24.2 (CH₃, C(CH₃)₂), 24.1 (CH₂, CH₂CHN), 18.4 (C_q, SiC(CH₃)₃), -5.3 (CH₃, SiCH₃), -5.4 (CH₃, SiCH₃). MS (LSIMS); m/z (%) : 396 [M+Na] (35), 374 [M+H] (100), 316 (7). HRMS [M+Na] C₁₈H₃₆NO₅Si : calcd. 374.236277; found 374.235950.

Bismesylate **19**.

To a solution of alcohol **16** (90.9 mg, 0.3 mmol), in pyridine (4.5 mL), was added TBDMSCl (136 mg, 0.9 mmol). The mixture was stirred at RT for 5h. The solution was washed with brine and then with a saturated solution of CuSO₄ to removed pyridine. The solvent was evaporated under vacuo. To a suspension of LiCl (52 mg, 1.22 mmol), and NaBH₄ (46 mg, 1.22 mmol) in THF (0.9 mL) at 0°C was added a solution of the crude azido ester in THF (1.1 mL). The mixture was warmed to RT and was stirred overnight. Saturated NH₄Cl

solution was added at 0°C, the mixture diluted with EtOAc and washed with saturated NH₄Cl solution and brine. The organic layers were dried over Na₂SO₄ and the solvent removed under vacuo. The residue was purified by flash chromatography (Petroleum ether/EtOAc : 7/3) to afford a colorless oil (95.2 mg, 82% over two steps). IR (neat) $\nu_{\max}$ = 3417 (OH), 2931 (CH), 2106 (CHN₃), 1257, 1166 cm⁻¹. ¹H NMR (CDCl₃, 300Mhz) δ 4.16 (dd, J = 5.6, 4.5 Hz, 1H, CHOCHN₃), 4.00 (m, 1H, CHO), 3.95 (br, 1H, CHOH), 3.83 (dd, J = 10.0, 2.8 Hz, 1H, CH₂OTBDMS), 3.71-3.59 (m, 4H, CHN₃, CH₂OTBDMS, CH₂OH), 2.81 (br, 1H, OH), 2.01 (br, 1H, OH), 1.87-1.67 (m, 4H, CH₂CH₂OH), 1.48 (s, 3H, C(CH₃)₂), 1.33 (s, 3H, C(CH₃)₂), 0.90 (s, 9H, SiC(CH₃)₃), 0.08 (s, 6H, Si(CH₃)₂). ¹³C NMR (CDCl₃, 75Mhz) δ 108.8 (C_q, OCO), 79.8 (CH, CHO), 76.2 (CH, CHO), 69.1 (CH, CHOH), 64.3 (CH₂, CH₂OTBDMS), 61.8 (CH₂, CH₂OH), 59.0 (CH, CHN₃), 29.1 (CH₂), 27.8 (CH₂), 27.0 (CH₃, C(CH₃)₂), 25.8 (CH₃, SiC(CH₃)₃), 24.8 (CH₃, C(CH₃)₂), 18.3 (C_q, SiC(CH₃)₃), -5.4 (CH₃, Si(CH₃)₂), -5.5 (CH₃, Si(CH₃)₂). MS (ESI); m/z (%) : 412 [M+Na] (100), 362 (82), 329 (8), 304 (16). HRMS (LSIMS) [M+Na] C₂₅H₄₁N₃O₄SiNa : calcd. 412.223579; found 412.224370.

To a cooled solution of the diol (109 mg, 0.28 mmol) in CH₂Cl₂ (1.7 mL) (0°C), was added Et₃N (0.09 mL, 1.12 mmol) and MsCl (0.16 mL, 1.12 mmol). The mixture was allowed to warm to RT and stirred for 3h. The reaction was quenched with brine and the aqueous layer extracted with CH₂Cl₂. The organic layer was washed with brine then dried over Na₂SO₄. The residue was purified through silica (Petroleum ether/EtOAc : 7/3) to afford a yellow oil (126 mg, 89%). IR (neat) $\nu_{\max}$ = 2950-2850 (CH), 2109 (CHN₃),

1257, 1176 cm^{-1} . ^1H NMR (CDCl_3 , 300MHz) δ 5.02 (m, 1H, CHOMs), 4.36 (m, 1H, CH_fO), 4.29 (m, 2H, CH_{a2}OMs), 4.20 (dd, $J = 6.8, 3.4$ Hz, 1H, CH_eO), 4.13 (dd, $J = 12.2, 2.1$ Hz, 1H, CH_{h2}O), 3.90 (dd, $J = 12.1, 4.5$ Hz, 1H, CH_{h2}O), 3.51 (m, 1H, CHN_3), 3.13 (s, 3H, CH_3SO_3), 3.02 (s, 3H, CH_3SO_3), 2.08-1.76 (m, 4H, 2 x CH_2), 1.52 (s, 3H, $\text{C}(\text{CH}_3)_2$), 1.34 (s, 3H, $\text{C}(\text{CH}_3)_2$), 0.91 (s, 9H, $\text{SiC}(\text{CH}_3)_3$), 0.10 (s, 6H, $\text{Si}(\text{CH}_3)_2$). ^{13}C NMR (CDCl_3 , 75MHz) δ 109.1 (C_q , OCO), 81.1 (CH, CHOMs), 78.8 (CH, C_eHO), 73.8 (CH, C_fHO), 69.0 (CH_2 , CH_2OMs), 62.2 (CH_2 , CH_2OTBDMS), 57.8 (CH, CHN_3), 39.6 (CH_3 , CH_3SO_3), 37.3 (CH_3 , CH_3SO_3), 27.3 (CH_2), 26.3 (CH_3 , $\text{C}(\text{CH}_3)_2$), 25.9 (CH_2), 25.8 (CH_3 , $\text{SiC}(\text{CH}_3)_3$), 24.3 (CH_3 , $\text{C}(\text{CH}_3)_2$), 18.3 (C_q , $\text{SiC}(\text{CH}_3)_3$), -5.5 (CH_3 , SiCH_3), -5.6 (CH_3 , SiCH_3). MS (LSIMS) m/z (%) : 568 (48) $[\text{M}+\text{Na}]$, 518 (100). HRMS $[\text{M}+\text{Na}]$ $\text{C}_{19}\text{H}_{39}\text{N}_3\text{O}_9\text{S}_2\text{SiNa}$: calcd. 568.179472; found. 568.179015.

(3aR,4S,8aR,8bS)-4-((tert-butyl dimethylsilyloxy)methyl)-2,2-dimethyl-hexahydro-3aH-[1,3]dioxolo[4,5-a]pyrrolizine **20**.

The dimesylate **19** (87 mg, 0.172 mmol) was diluted in EtOAc (1.4 mL), 10% Pd/C (10 mg) and Et_3N (0.12 mL, 0.86 mmol) was added. The mixture was stirred at RT under H_2 (1 atm) overnight. The solution was filtered through Celite (EtOAc, 20 mL). IR (neat) $\nu_{\text{max}} = 2930\text{--}2850$ (CH), 1099 cm^{-1} . ^1H NMR (CDCl_3 , 250 MHz) δ 4.74 (dd, $J = 5.9, 4.4$ Hz, 1H, CH_f), 4.48 (dd, $J = 5.3, 5.3$ Hz, 1H, CH_e), 4.00 (m, 2H, CH_{2h}), 3.26 (m, 1H, CH_d), 3.07 (m, 2H, CH_g , CH_a), 2.71 (m, 1H, CH_a), 2.10-1.85 (m, 4H, CH_{c2} , CH_{b2}), 1.45 (s, 3H, CH_3), 1.28 (s, 3H, CH_3), 0.91 (s, 9H, $\text{C}(\text{CH}_3)_3$), 0.09 (s, 6H, $\text{Si}(\text{CH}_3)_2$). ^{13}C NMR (C_6D_6 , 75 MHz) δ 112.0 (C_q , OCO), 85.3 (CH, C_fHO), 81.6 (CH, C_eHO), 69.8 (CH, C_dHN), 65.7 (CH, C_gHN), 61.5 (CH_2 , $\text{C}_h\text{H}_2\text{OSi}$), 48.0 (CH_2 , $\text{C}_a\text{H}_2\text{N}$), 27.7 (CH_2 , C_bH_2), 27.2 (CH_3 , $\text{C}(\text{CH}_3)_2$), 36.7 (CH_3 , $\text{C}(\text{CH}_3)_3$), 24.5 (CH_3 , $\text{C}(\text{CH}_3)_2$), 22.6 (CH_2 , C_cH_2), 19.2 (C_q , $\text{C}(\text{CH}_3)_3$), -4.6 (2x CH_3 , $\text{Si}(\text{CH}_3)_2$). MS (ESI); m/z (%) : 376 (70) $[\text{M}+\text{Na}]$, 328 (100) $[\text{M}+\text{H}]$. HRMS $\text{C}_{17}\text{H}_{34}\text{NO}_3\text{Si}$: calcd. 328.2308; found. 328.2294.

3-*epi*-hyacinthacine A₁ **21**.

The resulting filtrate was concentrated in vacuo and the crude product dissolved in MeOH/HCl (v/v : 2/1) (0.7 mL). The solution was stirred under reflux for 1h. The solvent was evaporated and the chlorhydrate was purified through DOWEX 1X10 (OH^- form) and eluted with water to afford a colorless oil (22.9 mg, 77% from **19**). $[\alpha_D]^{20} = +3.4^\circ$ ($C = 0.32$, H_2O). ^1H NMR (CD_3OD , 400MHz) δ 4.20 (t, $J = 4.6, 4.6$ Hz, 1H, H-2), 4.13 (dd, $J = 6.6, 4.6$ Hz, 1H, H-1), 3.94 (dd, $J = 11.6, 5.0$ Hz, 1H, H-8), 3.87 (dd, $J = 11.6, 6.0$ Hz, 1H, H-8'), 3.58 (m, 1H, H-7a), 3.26-3.15 (m, 2H, H-5, H-3), 2.95 (m, 1H, H-5'), 2.09 (m, 1H, H-7), 2.00 (m, 1H, H-6), 1.81-1.70 (m, 2H, H-6, H-7). ^{13}C NMR (CD_3OD , 75 MHz) δ 76.2 (CH, C-2), 73.3 (CH, C-1), 68.7 (CH, C-7a), 65.9 (CH, C-3), 59.5 (CH_2 , C-8), 50.1 (CH_2 , C-5), 28.6 (CH_2 , C-6), 26.5 (CH_2 , C-7). MS (ESI); m/z (%) : 174 (100) $[\text{M}+\text{H}]$. HRMS (LSIMS) $[\text{M}+\text{H}]$ $\text{C}_8\text{H}_{16}\text{NO}_3$: calcd. 174.113019, found. 174.112998.

(R)-methyl 4-azido-4-((4S,5S)-2,2-dimethyl-5-((S)-oxiran-2-yl)-1,3-dioxolan-4-yl)butanoate **22**.

To a solution of mesylate **17** (73 mg, 0.148 mmol) in THF (2.4 mL), was added TBAF (1M, 0.18 mL, 0.18 mmol) at RT. The mixture was stirred at RT for 2h. The organic layer was washed with brine. The solvent was evaporated under vacuo and the residue dissolved in MeOH (2.5 mL). Potassium carbonate (23 mg, 0.166 mmol) was added at RT and the resulting suspension was stirred overnight. Et₂O was added and the organic layer washed with water. The aqueous layer was extracted with Et₂O, the combined organic layers were washed with brine and dried over Na₂SO₄. The solvent was evaporated under vacuo and the residue purified through silica gel (petroleum ether/EtOAc : 7/3) to afford a colorless oil (29.6 mg, 70%). IR (neat) $\nu_{\max}$ = 2990-2939 (CH), 2109 (CHN₃), 1732 (ester), 1439, 1053 cm⁻¹. ¹H NMR (CDCl₃, 300MHz) δ 4.18 (dd, J = 6.8, 5.6 Hz, 1H, CH_eO), 3.85 (dd, J = 6.6, 6.6 Hz, 1H, CH_fO), 3.69 (s, 3H, CH₃O), 3.44 (m, 1H, CHN₃), 3.27 (m, 1H, CH_gO), 2.83 (m, 1H, CH_hO), 2.64 (dd, J = 4.9, 2.6 Hz, 1H, CH_hO), 2.53 (m, 2H, CH_{c2}), 1.99-1.83 (m, 2H, CH_{b2}), 1.55 (s, 3H, C(CH₃)₂), 1.35 (s, 3H, C(CH₃)₂). ¹³C NMR (CDCl₃, 75MHz) δ 173.0 (C_q, C=O), 109.7 (C_q, OCO), 79.8 (CH, C_eHO), 78.3 (CH, C_fHO), 59.6 (CH, CHN₃), 51.8 (CH₃, CH₃OOC), 50.1 (CH, C_gHO), 43.7 (CH₂, C_hH₂), 30.2 (CH₂, C_bH₂), 26.6 (CH₂, C_cH₂), 26.6 (CH₃, C(CH₃)₂), 24.8 (CH₃, C(CH₃)₂). MS (ESI); m/z (%) : 308 (100) [M+Na]. HRMS (LSIMS) C₁₂H₁₉N₃O₅Na : calcd. 308.122241; found. 308.122707.

(3aR,4R,8aR,8bS)-4-(hydroxymethyl)-2,2-dimethyl-tetrahydro-7H-[1,3]dioxolo[4,5-a]pyrrolizin-6(8bH)-one **23**.

The epoxide **22** (29.3 mg, 0.102 mmol) was dissolved in MeOH (1.1 mL) and 10% Pd/C (2 mg) was added. The suspension was stirred at RT under H₂ (1 atm) for 2h. The solution was filtered through Celite (MeOH, 10 mL) then the residue was concentrated under vacuo. The crude product was dissolved in MeOH (1.5 mL), Et₃N (0.07 mL, 0.51 mmol) was added and the solution was heated under reflux overnight. The solvent was evaporated and the residue purified through silica gel (DCM/MeOH : 98/2) to afford a yellow oil (22.2 mg, 96%). IR (neat) $\nu_{\max}$ = 3388 (OH), 2986-2936 (CH), 1673 (lactam) cm⁻¹. ¹H NMR (CDCl₃, 300 MHz) δ 4.79 (dd, J = 5.6, 1.1 Hz, 1H, H-2), 4.59 (dd, J = 5.5, 3.9 Hz, 1H, H-1), 4.17 (m, 1H, H-7a), 3.92 (m, 1H, H-3), 3.58 (m, 2H, H-8), 2.61 (m, 1H, H-6), 2.42 (m, 1H, H-6), 2.28-2.03 (m, 2H, H-7). ¹³C NMR (CDCl₃, 75 MHz) δ 179.8 (C_q, C=O), 112.9 (C_q, OCO), 86.1 (CH, C-2), 81.3 (CH, C-1), 65.5 (CH, C-7a), 64.3 (CH, C-3), 62.5 (CH₂, C-8), 34.1 (CH₂, C-6), 26.9 (CH₂, C-7), 24.6 (CH₃, C(CH₃)₂), 18.7 (CH₃, C(CH₃)₂). MS (ESI); m/z (%) : 250 (100) [M+Na]. HRMS (LSIMS) [M+H] C₁₁H₁₈NO₄ : calcd. 228.123583, found. 228.123624.

Hyacinthacine A₁ **3**.¹

A solution of LiAlH₄ (1M in Et₂O, 0.25 mL, 0.25 mmol), was added dropwise at 0°C to a solution of lactam **23** (22.7 mg, 0.1 mmol), in THF. The mixture was stirred under reflux for 1h. After cooling to 0°C, H₂O (0.01 mL), NaOH 10% (0.01 mL) and H₂O (0.03 mL) were

¹ Asano, N.; Kuroi, H.; Ikeda, K.; Kizu, H.; Kameda, Y.; Kato, A.; Adachi, I.; Watson, A. A.; Nash, R. J.; Fleet, G. W. J. *Tetrahedron: Asymmetry* **2000**, *11*, 1-8.

added. The aqueous layer was extracted with EtOAc (x 4) and the combined organic layers dried over Na₂SO₄. The crude mixture was purified through silica gel (DCM/MeOH : 95/5) to afford a colorless oil (16 mg, 75%).

The previous product (15 mg, 0.07 mmol) was dissolved in MeOH/HCl (v/v : 2/1) (0.8 mL). The solution was stirred under reflux for 1h. The solvent was evaporated and the chlorhydrate was purified through DOWEX 1X10 (OH⁻ form) and eluted with water to afford **3¹** as a colorless oil (10.5 mg, 87%). $[\alpha_D]^{20} = +45^\circ$ (C = 0.23, H₂O). ¹H NMR (CD₃OD, 400 MHz) δ 3.89–3.84 (m, 2H, H-1, H-2), 3.80 (dd, *J* = 11.2, 3.1 Hz, 1H, H-8), 3.58 (dd, *J* = 11.0, 6.6 Hz, 1H, H-8'), 3.46 (m, 1H, H-7a), 3.06 (m, 1H, H-5), 2.77 (m, 1H, H-3), 2.65 (m, 1H, H-5), 2.09 (m, 1H, H-7), 1.94 (m, 1H, H-6), 1.77 (m, 1H, H-6), 1.70 (m, 1H, H-7). ¹³C NMR (CDCl₃, 75 Mhz) δ 77.5 (CH, C-8), 73.4 (CH, C-7), 71.9 (CH, C-6), 67.8 (CH, C-5), 65.3 (CH₂, C-4), 57.6 (CH₂, C-3), 28.8 (CH₂, C-2), 26.0 (CH₂, C-1). MS (ESI); *m/z* (%) : 174 (100) [M+H]. HRMS (LSIMS) [M+H] C₈H₁₆NO₃: calcd. 174.113019, found. 174.112872.

lc364.1
GA3762
300-CDCL3

S13

C₁₉H₂₈O₄Si (348,51 g/mol)

10a

C₁₉H₂₈O₄Si (348,51 g/mol)

10b $C_{24}H_{30}O_4Si$ (410,58 g/mol)

S16

C₁₉H₃₀O₄Si (350,52 g/mol)

10c

C₁₉H₃₀O₄Si (350,52 g/mol)

10c

LC394.1
Carbone

12

C₁₉H₂₈O₄Si (348,51 g/mol)

173.2291
170.6254

137.8241
133.8022
129.1693
127.8456

112.4050

90.7678

82.5857

72.2798

60.2066

34.3875

28.1327
26.7944
26.0235
25.8853
25.2962
20.9179
14.2049
9.32

-3.2358
-3.6576

15a-15b $C_{15}H_{25}N_3O_7$ (359,37 g/mol)

$\text{C}_{17}\text{H}_{27}\text{N}_3\text{O}_8$ (401,41 g/mol)

173.7892

108.9139

79.9747

77.1964

69.1743

64.5777

58.7229

51.9227

30.3728

27.1799

26.8235

25.0271

S37

16

$$\text{C}_{19}\text{H}_{37}\text{N}_3\text{O}_8\text{SSi} \text{ (495,66g/mol)}$$

— 173.1469

17

C₁₉H₃₇N₃O₈SSi (495,66g/mol)

— 109.1298

— 81.2001

— 78.9257

— 74.3314

— 62.2922

— 58.1982

— 51.7995

— 39.1842

— 30.3443

26.5839

26.2655

25.8106

24.4005

18.3354

S39

-5.5004

-5.5611

(ppm)

19

S42

— 108.8412

— 79.7856

— 76.2000

— 69.0797

— 64.3450

— 61.8576

— 59.0211

— 29.1073

— 27.8418

— 26.9763

— 25.8344

— 24.8598

— 18.2850

— 5.3886

— 5.4977

LC690.0

20

CDCl_3

$\text{C}_{17}\text{H}_{33}\text{NO}_3\text{Si}$ (327,53 g/mol)

20 C_6D_6 $C_{17}H_{33}NO_3Si$ (327,53 g/mol)

21 $C_8H_{15}NO_3$ (173,21 g/mol)

C₈H₁₅NO₃ (173,21 g/mol)

HSQC/ LC781.1 /CD3OD

23

C₁₁H₁₇NO₄ (227,26 g/mol)

C₁₁H₁₇NO₄ (227,26 g/mol)

lc817.b

620

23

C₁₁H₁₇NO₄ (227,26 g/mol)

NOESY/ LC817-1 /CD3OD mix=400ms

23

$C_{11}H_{17}NO_4$ (227,26 g/mol)

3 $C_8H_{15}NO_3$ (173,21 g/mol)

3

 $C_8H_{15}NO_3$ (173,21 g/mol)

$C_8H_{15}NO_3$ (173,21 g/mol)