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Angewandte Chemie, **1999**

Supporting Information for:

Asymmetric Total Synthesis of Fluvirucinine A_1**

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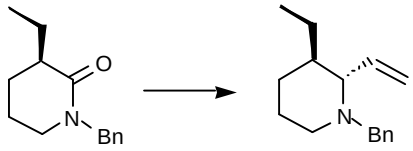
Experimental section

Unless noted otherwise, all starting materials were obtained from commercial suppliers and were used without further purification. Tetrahydrofuran and Et_2O were distilled from sodium benzophenone ketyl. N,N-Dimethylformamide was distilled under reduced pressure from calcium hydride and stored over 4 Å molecular sieves under argon. Dichloromethane, triethylamine, benzene, toluene, acetonitrile and pyridine were freshly distilled from calcium hydride. All solvents used for routine isolation of products and chromatography were reagent grade and glass distilled. Reaction flasks were dried at 120 ^oC. Air and moisture sensitive reactions were performed under an argon atmosphere. Flash column chromatography was performed using silica gel 60 (230-400 mesh, Merck) with indicated solvents. Thin-layer chromatography was performed using 0.25 mm silica gel plates(Merck). Melting points were measured on a Büchi melting point apparatus and are uncorrected. Optical rotations were measured with JASCO DIP-1000 digital polarimeter at ambient temperature using 100 mm cell of 2mL capacity. Infrared spectra were recorded on a Perkin-Elmer 1710 FT-IR spectrometer. Mass spectra were obtained with VG Trio-2 GC-MS instrument. High-resolution mass spectra were obtained with JEOL JMS-AX 505WA instrument. ^1H and ^{13}C NMR spectra were recorded on either a JEOL JNM-GCX 400 or JEOL JNM-LA 300 spectrometer as solutions in deuteriochloroform($CDCl_3$). Chemical shifts are expressed in parts per million (ppm, *d*) downfield from tetramethylsilane and are referenced to the deuterated solvent($CHCl_3$). ^1H-NMR data were reported in the order of chemical shift, multiplicity(s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet and/or multiple resonance), number of protons, and coupling constant in hertz(Hz).

Diastereoselective vinylation of benzyl-protected 3-ethylvalerolactam(8-1)



8-1 **9**

To a solution of $LiAl(EtO)_3H$ (1.25 M solution in ethyl ether, 7.7 mL, 9.7 mmmol) was added benzyl-protected 3-ethylvalerolactam **8-1** (1.75 g, 8.1 mmol) in 100 mL of ethyl ether at 0 ^oC and the mixture was stirred for 30 min. Vinylmagnesium bromide (1.0 M in THF, 24.0 mL, 24.0 mmol) was added to the reaction mixture and stirred for 24 h at 0 ^oC. After evaporation of the solvent, the residue was diluted with EtOAc (100 mL). The solution of potasium sodium tartrate tetrahydrate (15% in H_2O, 40 mL) was added and the mixture was stirred for 2h at room temperature. The organic phase was washed with water and brine, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (20:1 hexane:EtOAc) to afford *trans*-2,3-disubstituted piperidine **9** (1.29g, 70%) as a clear liquid.

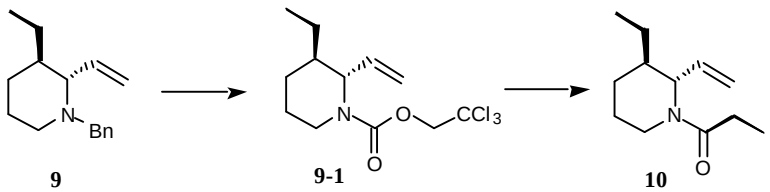
***trans* isomer**

IR (neat) 3065, 2930, 2800, 1495, 1450 cm^{-1} ; ^{1}H-NMR ($CDCl_3$, 300 MHz): *d* 7.26-7.15 (m, 5H), 5.64 (ddd, 1H, *J* = 17.3, 10.2, 9 Hz), 5.17 (dd, 1H, *J* = 10.2, 2.0 Hz), 5.08 (dd, 1H, *J* = 17.3, 2.0 Hz), 4.06 (d, 1H, *J* = 13.7 Hz), 2.91 (d, 1H, *J* = 13.7 Hz), 2.74 (m, 1H), 2.27 (t, 1H, *J* = 9.3 Hz), 1.80-1.75 (m, 1H), 1.79 (dt, 1H, *J* = 11.7, 3.2 Hz), 0.79 (t, 3H, *J* = 7.6 Hz); ^{13}C-NMR ($CDCl_3$, 75 MHz): *d* 140.9, 139.9, 128.9, 127.9, 126.5, 117.9, 71.8, 59.8, 52.1, 41.4, 28.6, 25.7, 25.0, 11.0; $[\alpha]^{20}_D$ +57.1 (*c* 2.0, CH_2Cl_2); HRMS (EI) Calcd for $C_{16}H_{23}N$: 229.1831 Found: 229.1826

***cis* isomer**

IR (neat) 3065, 3027, 2926, 2957, 2795, 1495, 1454 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 300 MHz): *d* 7.27-7.12 (m, 5H), 5.95 (ddd, 1H, *J* = 17.0, 10.3, 10.0 Hz), 5.20 (dd, 1H, *J* = 2.5, 10.3 Hz), 4.98 (dd, 1H, *J* = 17.0 Hz), 3.48 (d, 1H, *J* = 14.7 Hz), 3.38 (d, 1H, *J* = 13.7 Hz), 3.07 (dd, 1H, *J* = 10.0, 4.1 Hz), 2.41-2.37 (m, 2H), 1.64-1.48 (m, 4H), 1.21-1.01 (m, 3H), 0.77 (t, 3H, *J* = 7.3 Hz); MS (EI) 229 (M^+)

Conversion of trans-3-ethyl-2-vinylpiperidine 9 to 1-propionyl-2-vinylpiperidine 10



9 **9-1** **10**

Carbamate intermediate **9-1**

To a solution of trans-disubstituted piperidine **9** (2.66 g, 11.6 mmol) in 10mL of CH_3CN was added dropwise trichloro-ethylchloroformate (1.9 mL, 13.9 mmol). The resulting solution was refluxed for

2 h. After evaporation of the solvent, the residue was diluted with EtOAc (150 mL) and the organic phase was washed with water and brine, dried over $MgSO_4$ and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (20:1 hexane:EtOAc) to afford carbamate **9-1** (2.70 g, 74 %) as a colorless oil.

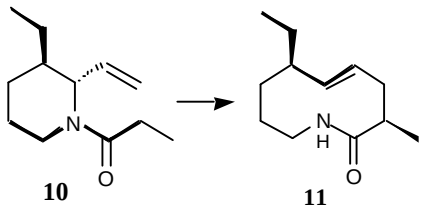
IR (neat) 2938, 1715, 1424, 1253 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 300 MHz): *d* 5.82 (ddd, 1H, *J* = 17.3, 10.5, 4.4 Hz), 5.21 (ddd, 1H, *J* = 10.5, 2.2, 1.2 Hz), 5.11 (ddd, 1H, *J* = 17.3, 2.2, 1.2 Hz), 4.78 (m, 1H), 4.72 (bs, 2H), 4.04 (m, 1H), 2.98 (m, 1H), 1.73-1.41 (m, 7H), 0.93 (t, 3H, *J* = 7.3 Hz); ^{13}C-NMR ($CDCl_3$, 100 MHz): *d* 154.5, 136.6, 116.2, 77.2, 75.0, 56.8, 40.0, 38.9, 24.0, 23.2, 19.9, 12.2; MS (EI) 314 (M^+); $[\alpha]^{20}_D$ +26.7 (*c* 0.89, CH_2Cl_2); HRMS (EI) Calcd for $C_{12}H_{18}NO_2Cl_3$: 313.0403 Found: 313.0400

3-Ethyl-1-propionyl-2-vinylpiperidine **10**

To a solution of carbamate **9-1** (2.70 g, 8.6 mmol) in acetic acid (10 mL) was added Zn powder (500 mg) and the mixture was stirred for 3 h at room temperature. The reaction mixture was filtered through celite pad and extracted with CH_2Cl_2 (100 mL) and the combined extracts were concentrated under reduced pressure to afford amine salt. To a solution of crude amine salt and DMAP (cat. amount) in CH_2Cl_2 (15 mL) was added triethylamine (3.6 mL, 25.8 mmol) and propionic anhydride (1.6 mL, 12.9 mmol). The resulting solution was stirred for 24 h. After evaporation of the solvent, the residue was diluted with ethyl ether (100 mL). The organic phase was washed with water and brine, dried over $MgSO_4$ and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (3:1 hexane:EtOAc) to afford 3-ethyl-1-propionyl-2-vinylpiperidine **10** (1.31 g, 78 %) as a colorless oil.

IR (neat) 2980, 1650, 1440 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 300 MHz): *d* 5.75-5.71 (m, 1H), 5.14-5.12 (m, 1.5H), 4.98 (d, 1H, *J* = 17.2 Hz), 4.50 (m, 0.5H), 4.19 (m, 0.5H), 3.53 (m, 0.5H), 3.09 (m, 0.5H), 2.60 (m, 0.5H), 2.21-2.33 (m, 2H), 1.20-1.98 (m, 7H), 1.08 (m, 3H), 0.87 (t, 3H, *J* = 7.4 Hz); MS (EI) 195 (M^+)

Conversion of 3-ethyl-1-propionyl-2-vinyl piperidine 10 to the lactam 11 by amide enolate-included aza-Claisen rearrangement

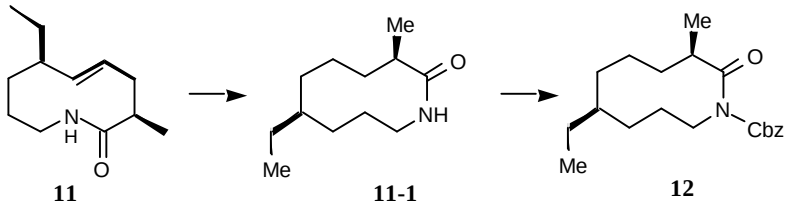


10 **11**

To a solution of LHMDS (7.6 mL of 1 M solution in hexane, 7.6 mmol) was added dropwise 3-ethyl-1-propionyl-2-vinyl piperidine **10** (1.23 g, 6.3 mmol) in toluene (30 mL) at 120 ^{o}C and the resulting solution was refluxed for 2 h. After addition of water (0.1 mL), the solvent was evaporated and the residue was purified by flash column chromatography on silica-gel (3:3:1 EtOAc: hexane: CH_2Cl_2) to give the pure lactam **11** (910 mg, 74 %) as a white solid.

mp 165-167 ^{o}C ; IR (KBr) 3315, 1646, 1556, 1448, 1250 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 300 MHz): *d* 5.34 (ddd, 1H, *J* = 15.6, 9.75, 4.5 Hz), 5.09 (dd, 1H, *J* = 15.3, 9.5 Hz), 4.81 (bs, 1H), 3.65 (m, 1H), 2.80 (m, 1H), 2.23-1.78 (m, 4H), 1.69-1.17 (m, 6H), 1.13 (d, 3H, *J* = 6.3 Hz), 0.79 (dt, 3H, *J* = 7.3 Hz); ^{13}C-NMR ($CDCl_3$, 100 MHz): *d* 175.4, 139.0, 127.1, 46.3, 44.3, 40.5, 39.2, 36.5, 28.4, 27.9, 15.9, 12.1; $[\alpha]^{20}_{D}$ -61.1 (*c* 0.6, CH_2Cl_2); MS (EI) 195 (M^+); HRMS (EI) Calcd for $C_{12}H_{21}NO$: 195.1623 Found: 195.1626

Conversion of the lactam 11 to the *N*-cbz-protected lactam 12



11 **11-1** **12**

Lactam intermediate **11-1**

A solution of the lactam **11** (700 mg, 3.58 mmol) and 10% Pd/C (100 mg) in 20 mL of anhydrous MeOH was placed under an atmosphere of hydrogen. After stirring for 18 h, the reaction mixture was diluted with EtOAc (50 mL), filtered through celite pad and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (EtOAc only) to afford the hydrogenated lactam **11-1** (700 mg, 99 %) as a white solid.

mp 140-142.2 ^{o}C; IR (neat) 3435, 1645, 1550 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 300 MHz): *d* 5.55 (bs, 1H), 3.73-3.64 (m, 1H), 2.78-2.71 (m, 1H), 2.16-2.09 (m, 1H), 1.88-1.79 (m, 1H), 1.71-1.05 (m, 12H), 1.04 (d, 3H, *J* = 6.7Hz), 0.78 (t, 3H, *J* = 7.3 Hz); ^{13}C-NMR ($CDCl_3$, 100 MHz): *d* 176.5, 41.8, 40.3, 39.8, 33.7, 30.2, 28.2, 27.3, 23.7, 21.6, 16.8, 12.0; MS (EI) 197 (M^+); HRMS (EI) Calcd for $C_{12}H_{23}NO$: 197.1779 Found: 197.1778

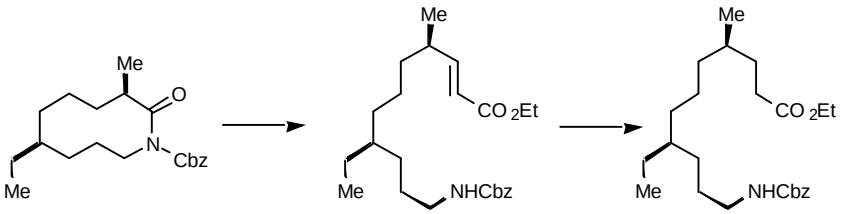
N-Cbz-lactam **12**

To a solution of the hydrogenated lactam **11-1** (550 mg, 2.8 mmol) in THF (15 mL) was added *n*-BuLi (1.6 M in hexane, 1.9 mL, 3.1 mmol) at -78 ^{o}C. After the mixture was stirred at -78 ^{o}C for 10min, benzyl chloroformate (0.48 mL, 3.35 mmol) was added and the mixture was stirred at -78 ^{o}C for 2 h. The reaction mixture was quenched by adding saturated NH_4Cl (5 mL), and the mixture was allowed to warm to room temperature. The organic layer was separated, and the aqueous layer was

extracted with CH_2Cl_2 (3x15 mL). The combined organic layers were dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (3:1 hexane:EtOAc) to afford the *N*-cbz-lactam **12** (869 mg, 94 %) as a colorless oil.

IR (neat) 2930, 1740, 1700, 1500, 1390 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 300 MHz): *d* 7.38-7.32 (m, 5H), 5.16 (ABq, 2H, *J* = 17.2, 12.0 Hz), 4.16 (ddd, 1H, *J* = 13.6, 9.0, 4.2 Hz), 3.59-3.50 (m, 2H), 1.68-1.48 (m, 5H), 1.34-1.29 (m, 3H), 1.13-0.96 (m, 5H), 1.06 (d, 3H, *J* = 6.8 Hz), 0.69 (t, 3H, *J* = 6.8 Hz); ^{13}C-NMR ($CDCl_3$, 100 MHz): *d* 181.3, 154.9, 135.3, 128.6, 128.5, 128.3, 68.3, 45.9, 41.2, 37.6, 31.3, 30.5, 29.3, 28.8, 23.7, 20.5, 16.7, 11.7; $[\alpha]^{20}_D$ -56.4 (*c* 1.05, CH_2Cl_2); MS (EI) 331 (M^+); HRMS (CI) Calcd for $C_{20}H_{30}NO_3$ (M+H): 332.2226 Found: 332.2227

Conversion of the *N*-cbz-protected lactam 12 to the saturated ester 13



Ester intermediate **12-1**

Diisobutyl aluminum hydride(1.0 M solution in toluene, 3.7 mL, 3.7 mmol) was very slowly added to the *N*-cbz-lactam **12** (1.10 g, 3.3 mmol) in 20 mL of CH_2Cl_2 at -78 ^{o}C. After 1 h at -78 ^{o}C, the reaction mixture was quenched with a solution of potassium sodium tartrate tetrahydrate (15% in H_2O, 15 mL). The aqueous layer was extracted with EtOAc (2x30 mL) and the combined extracts were washed with brine and dried over $MgSO_4$. Concentration of the organic layer under reduced pressure affords the crude aldehyde.

To a solution of the crude aldehyde in 30mL of CH_2Cl_2 was added (carbethoxymethylene) triphenylphosphorane (1.50 g, 4.3 mmol) in one portion. The mixture was stirred for 6 h. The solvent was evaporated and the residue was purified by flash column chromatography on silica gel (5:1 hexane:EtOAc) to afford ester **12-1** (857 mg, 68 %) as a clear oil.

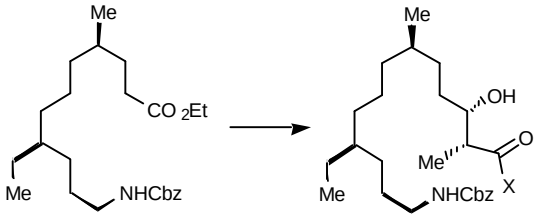
IR (neat) 3400, 2930, 1716, 1651, 1541 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 300 MHz): *d* 7.37-7.25 (m, 5H), 6.83 (dd, 1H, *J* = 15.6, 7.8 Hz), 5.64 (dd, 1H, *J* = 15.6, 1.2 Hz), 5.07 (s, 2H), 4.78 (bs, 1H), 4.18 (q, 2H, *J* = 7.1 Hz), 3.14 (q, 2H, *J* = 6.8 Hz), 2.26 (m, 1H), 1.98-1.19 (m, 13H), 1.26 (t, 3H, *J* = 7.1 Hz), 1.01 (d, 3H, *J* = 6.6 Hz), 0.79 (t, 3H, *J* = 7.1 Hz); ^{13}C-NMR ($CDCl_3$, 100 MHz): *d* 166.9, 156.3, 154.6, 136.6, 128.4, 128.0, 119.6, 66.5, 60.1, 41.5, 38.4, 36.4, 36.3, 33.0, 30.1, 27.2, 25.6, 24.1, 19.4, 14.2, 10.7; $[\alpha]^{20}_D$ -20.6 (*c* 0.22, CH_2Cl_2); MS (EI) 403 (M^+); HRMS (EI) Calcd for $C_{24}H_{37}NO_4$: 403.2723 Found: 403.2725

Saturated ester **13**

Reduction of ester **12-1** (800 mg, 19.8 mmol) was performed with $NaBH_4$(757 mg, 20.0 mmol) in the presence of Cu_2Cl_2 (99 mg, 1.0 mmol) in 4 mL of MeOH/THF (3/1) at 0 ^oC for 2 h. The reaction mixture was filtered through celite pad and extracted with Et_2O (2x30 mL). The extract was washed with water, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (5:1 hexane:EtOAc) to afford the saturated ester **13** (763 mg, 95 %) as a clear oil.

IR (neat) 3385, 2850, 1717, 1700, 1522, 1458 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 300 MHz): *d* 7.34-7.28 (m, 5H), 5.07 (s, 2H), 4.76 (bs, 1H), 4.09 (q, 2H, *J* = 7.1 Hz), 3.15 (m, 2H), 2.30-2.23 (m, 2H), 1.68-1.40 (m, 5H), 1.22 (dt, 3H, *J* = 7.1, 0.7 Hz), 1.25-1.18 (m, 11H), 0.84 (d, 3H, *J* = 6.3 Hz), 0.80 (t, 3H, *J* = 7.1 Hz); ^{13}C-NMR ($CDCl_3$, 75 MHz): *d* 173.7, 156.2, 136.6, 128.1, 127.72, 127.66, 66.1, 59.9, 41.2, 38.3, 36.8, 33.0, 32.1, 31.8, 31.6, 29.9, 26.9, 25.5, 23.6, 19.0, 14.0, 10.5; $[\alpha]^{20}_D$ +0.8 (*c* 1.5, CH_2Cl_2); MS (EI) 405 (M^+); HRMS (CI) Calcd for $C_{24}H_{40}NO_4$ (M+H): 406.2957 Found: 406.2951

Conversion of the saturated ester 13 to the aldol intermediate 14



13 **14**

Aldol intermediate **14**

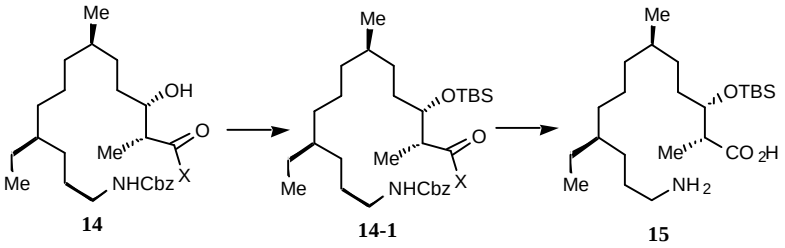
Diisobutyl aluminum hydride (1.0 M solution in toluene, 1.9 mL, 1.9 mmol) was added to the saturated ester **13** (700 mg, 1.7 mmol) in 20 mL of CH_2Cl_2 at -78 ^oC. After 1h at -78 ^oC, the reaction mixture was quenched with potassium sodium tartrate tetrahydrate (15 % in H_2O, 15 mL). The aqueous layer was extracted with EtOAc (2x30 mL) and the combined extracts were washed with brine and dried over $MgSO_4$. Concentration of the organic layer under reduced pressure affords the crude aldehyde.

Di-*n*-butyl triflate(1.0 M in CH_2Cl_2, 1.8 mL, 1.8 mmol) was added dropwise with stirring to a solution of (4R,5S)-3-propionyl-4-methyl-5-phenyloxazolidin-2-one (419 mg, 1.8 mmol) in 30 mL of CH_2Cl_2 at -78 ^oC. After addition of triethylamine (0.29 mL, 2.1 mmol), and the reaction mixture was stirred for 1 h at -78 ^oC and then for 1 h at 0 ^oC. The reaction mixture was cooled to -78 ^oC and a solution of the aporementioned crude aldehyde in CH_2Cl_2 (10 mL) was added dropwise. The reaction mixture was stirred at -78 ^oC for 30 min and then at 0 ^oC for 1 h, whereupon the reaction was quenched by an addition of 0.25 M aqueous NaH_2PO_4 (pH = 7, 1.2 mL). MeOH was added until the mixture became homogeneous. The solution was cooled to 0 ^oC and a mixture (1:1) of MeOH and

30% H_2O_2 (total volume of 2.7 mL) was added while the internal temperature was maintained below 5 °C. The resulting solution was stirred for 2h at room temperature. The organic solvents were removed under reduced poressure, and the aqueous layer was extracted with CH_2Cl_2 (3 x 30 mL). The combined organic layers were washed with saturated $NaHCO_3$ (10 mL), dried over $MgSO_4$ and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (2:1 hexane:EtOAc) to afford aldol intermediate **14** (648 mg, 79 %) as a clear oil.

IR (neat) 3450, 2920, 1780, 1700, 1540, 1455 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 300 MHz): *d* 7.43-7.27 (m, 10H), 5.65 (d, 1H, *J* = 7.3 Hz), 5.07 (s, 2H), 4.77 (m, 2H), 3.91 (m, 1H), 3.76 (qd, 1H, *J* = 7.0, 2.7 Hz), 3.15 (q, 2H, *J* = 6.6 Hz), 2.91, (bs, 1H), 1.57-1.09 (m, 18H), 1.22 (d, 3H, *J* = 7.1 Hz), 0.864 (d, 3H, *J* = 6.6 Hz), 0.856 (d, 3H, *J* = 6.4 Hz), 0.81 (t, 3H, *J* = 7.0 Hz); ^{13}C-NMR ($CDCl_3$, 75 MHz) *d* 177.4, 156.4, 152.6, 136.7, 133.1, 128.8, 128.7, 128.5, 128.1, 128.0, 125.6, 78.9, 71.8, 66.5, 54.7, 42.1, 41.5, 38.5, 37.3, 33.3, 33.1, 32.6, 31.3, 30.1, 27.1, 25.8, 23.9, 19.6, 14.3, 10.8, 10.2; $[\alpha]^{20}_D$ +12.5 (*c* 0.1, CH_2Cl_2); MS (EI) 594 (M^+)

Conversion of the aldol intermediate 14 to the amino-acid 15 as a cyclization precursor



Silyl ether intermediate **14-1**

To a solution of aldol intermediate **14** (537 mg, 0.9 mmol) in CH_2Cl_2 (3 mL) at -78 °C was added 2,6-lutidine (0.21 mL, 1.8 mmol) and TBS triflate (0.25 mL, 1.1 mmol). The reaction mixture was stirred at -78 °C for 1h. Et_2O (50 mL) was then added, and the mixture was washed with water and brine (5 mL), dried over $MgSO_4$ and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (3:1 hexane:EtOAc) to afford the silyl ether **14-1** (429 mg, 67 %) as a colorless oil.

IR (neat) 3350, 2928, 1782, 1705, 1456, 1345 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 300 MHz): *d* 7.42-7.27 (m, 10H), 5.58 (d, 1H, *J* = 6.8 Hz), 5.07 (s, 2H), 4.68 (m, 2H), 3.98 (q, 1H, *J* = 5.6 Hz), 3.98-3.80 (m, 1H), 3.15 (q, 2H, *J* = 6.6 Hz), 1.53-0.78 (m, 27 H), 1.15 (d, 3H, *J* = 6.8 Hz), 0.88 (s, 9H), 0.04 (s, 3H), 0.02 (s, 3H); $[\alpha]^{20}_D$ -2.7 ° (*c* 0.085, CH_2Cl_2); MS (EI) 651 ($M-C_4H_9$)

Amino-acid **15**

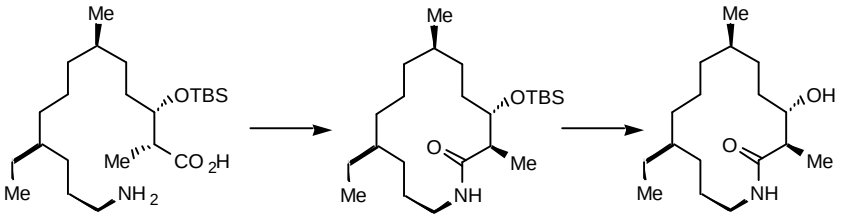
A solution of the silyl ether **14-1** (429 mg, 0.61 mmol) in 4mL of THF /H_2O (3/1) was treated at 0 °C with 30% H_2O_2 (0.28 mL) and then LiOH (29 mg, 1.22 mmol). The resulting mixture was stirred at 0

^{o}C for 2 h and the excess peroxide was quenched with 1.5 N aqueous Na_2SO_3 (10 % excess). The organic solvents were removed under reduced pressure, and the aqueous layer was extracted with CH_2Cl_2 (3x50 mL). The combined organic layers were dried over $MgSO_4$ and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (3:1 hexane:EtOAc) to afford silyloxy-acid intermediate (238 mg, 72 %) as a colorless oil.

IR (neat) 3333, 2928, 1713, 1537, 1462 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 300 MHz): *d* 7.37-7.28 (m, 5H), 5.08 (s, 2H), 4.76 (bs, 1H), 3.87 (m, 1H), 3.15 (q, 2H, *J* = 6.6 Hz), 2.59 (m, 1H), 1.48-0.78 (m, 24H), 1.12 (d, 3H, *J* = 6.8 Hz), 0.89 (s, 9H), 0.09 (s, 3H), 0.08 (s, 3H); MS (EI) 492 (M-C_4H_9)

A solution of silyloxy-acid intermediate (175 mg, 0.32 mmol) and 10% Pd/C (5 mg) in MeOH (10 mL) was placed under an atmosphere of hydrogen. After stirring for 2 h, the reaction mixture was diluted with EtOAc (20 mL), filtered through celite pad and concentrated under reduced pressure to give the crude amino-acid **15** as a viscous oil.

Conversion of the amino-acid 15 to fluvirucinine A_1(1)



15 **15-1** **1**

Lactam intermediate **15-1**

To a solution of amino-acid **15** (132 mg, 0.32 mmol) in CH_2Cl_2 (60 mL) was added Et_3N (0.22 mL, 1.6 mmol), pentafluorophenol (176 mg, 0.96 mmol) and *N*-[3-(dimethylamino) propyl]-*N*'-ethylcarbodiimide hydrochloride (307 mg, 1.6 mmol). The reaction mixture was stirred overnight at room temperature and then concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel (4:1 hexane:EtOAc) to give the lactam **15-1** (178 mg, 62 %) as a white solid.

mp 210-213 ^{o}C; IR (KBr) 3320, 1636, 1556 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 300 MHz): *d* 6.63 (bd, 1H, *J* = 7.6 Hz), 4.01-3.94 (m, 1H), 3.76-3.70 (m, 1H), 2.57-2.41 (m, 2H), 1.78-0.81 (m, 18H), 1.10 (d, 3H, *J* = 7.1 Hz), 0.91 (s, 9H), 0.84 (d, 3H, *J* = 6.8 Hz), 0.83 (t, 3H, *J* = 7.1 Hz), 0.09 (s, 3H), 0.08 (s, 3H); ^{13}C-NMR ($CDCl_3$, 100 MHz): *d* 173.8, 74.8, 46.0, 38.94, 38.87, 35.0, 32.1, 30.6, 27.5, 27.3, 27.0, 25.9, 24.1, 23.8, 23.4, 20.8, 18.0, 14.4, 11.9, -4.5, -4.6; $[\alpha]^{20}_{D}$ +125.0 (*c* 0.08, CH_3OH); MS (EI) 397 (M^{+}); HRMS (EI) Calcd for $C_{19}H_{38}NO_2Si$ (M-C_4H_9): 340.2672 Found: 340.2672

Fluvirucinine A_1 (**1**)

To a solution of lactam the **15-1** (50 mg, 0.13 mmol) in THF (5 mL) was added TBAF (1.0 M solution in THF, 0.2 mL) and the reaction was stirred at room temperature for 1 h. The solvent was removed under reduced pressure, and the residue was purified by flash column chromatography on silica gel (10:1 EtOAc:MeOH) to afford Fluvirucinine A_1 (35 mg, 98 %) as a white solid.

mp 232-238 ^{o}C; IR (KBr) 3305, 2918, 1637, 1541 cm^{-1}; ^{1}H-NMR ($CDCl_3$:CD_3OD = 1:1, 300 MHz): *d* 3.53-3.47 (m, 1H), 3.40-3.35 (m, 1H), 2.71 (m, 1H), 2.09 (dq, 1H, *J* = 9.5, 6.8 Hz), 1.55-0.89 (m, 18H), 1.05 (d, 3H, *J* = 6.8 Hz), 0.78 (d, 3H, *J* = 6.8 Hz), 0.72 (t, 3H, *J* = 7.1 Hz); ^{13}C-NMR ($CDCl_3$:CD_3OD = 1:1, 100 MHz): *d* 176.1, 73.1, 48.0, 38.3, 36.8, 31.9, 31.7, 31.3, 30.8, 30.1, 26.9, 26.2, 25.5, 20.3, 18.8, 14.1, 10.5; $[\alpha]^{20}_{D}$ +140.5, (*c* 0.1, CH_3OH); MS (EI) 283 (M^+); HRMS (EI) Calcd for $C_{17}H_{33}NO_2$: 283.2511 Found 283.2514