Supporting Information

Total Synthesis of (–)- α -Kainic Acid by (–)-Sparteine-Mediated Asymmetric Deprotonation/Cycloalkylation

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General. All moisture-sensitive reactions were carried out under an atmosphere of argon in flame-dried glassware with dried solvents. The solvents (THF, toluene, CH_2Cl_2 , CH_3CN , dimethyl sulfoxide, acetone, Et_2O , etc...) were dried according to standard procedures and distilled prior to use. Flash chromatography was performed using Merck silica gel 60 (particle size 0.040-0.055 mm, 230-400 mesh) at a pressure of about 1.5 bar. Solvents for chromatography, diethyl ether (Et_2O), petroleum ether (PE) and ethyl acetate (EtOAc) were distilled prior to use. For analytic thin layer chromatography (TLC), Merck plastic sheets (60F₂₅₄ silica gel) were used. Visualization was accomplished with UV light or by staining with a basic I_2 , permanganate, vanillin or cerium molybdate solutions. NMR spectra were recorded on a Bruker ARX 300 and AMX 400 and on a Varian Unity plus (Varian Inc., Palo Alto CA, USA) 600 spectrometer. Chemical shifts are given in ppm (δ) and J values are in Hz, with TMS (^1H) and CDCl_3 (^{13}C) as internal standards. The multiplicities are indicated by s (singlet), br.s (broad singlet), d (doublet), br.d (broad doublet), t (triplet), q (quartet), quin (quintet), m (multiplet). Infrared (IR) spectra were recorded on a Nicolet FT-IR 5DXC spectrometer. Optical rotations were measured at 20 °C with a Perkin-Elmer 341 at the sodium D line. Mass spectra and elemental analyses were performed at the Chemistry Department of the University of Münster. Exact mass determination (MS-ESI) was carried out with a Quattro LCZ (Waters-Micromass, Manchester, UK) with manospay inlet.

(2S)-2-Benzylamino-3-(tert-butyldimethylsilyloxy)-1-propanol (4) To a 2 M solution of LiBH_4 (9.16 ml, 18.32 mmol) in THF, a solution of O-TBS-*N*-benzyl-D-serine methyl ester (**3**) (10.65 g, 32.97 mmol) in THF/toluene (4:1) (50 ml) was slowly added. Toluene was added to avoid caking of the residue and to serve as a heat-transfer medium. The reaction mixture was heated at 100 °C for 20 min and then treated with saturated NH_4Cl . The aqueous phase was extracted with AcOEt (3x50 ml) and the combined organic phases were dried (MgSO_4) and concentrated *in vacuo*. The crude product was purified by flash chromatography, R_f 0.23 (AcOEt) affording **4** (4.65 g, 47%, 84% related to **3**) as a colourless oil. $[\alpha]_D^{20}$ –8.2 (c 1.10, CHCl_3). IR (film): ν/cm^{-1} = 3245-3503 (OH), 2790-2986, 1448, 1231. ^1H NMR (CDCl_3 , 300 Mz) δ : 0.02 (s, 6H, $\text{Si}(\text{CH}_3)_2$), 0.89 (s, 9H, $\text{Si}(\text{CH}_3)_3$), 2.20 (br s, 1H, NH), 3.75 (m, 1H, CHCH_2OH), 3.41 (dd, 1H, J = 4.7 and 10.8 Hz, CH_2OSi), 3.55 (m, 3H, CH_2OH and CH_2OSi), 3.69 (s, 2H, NCH_2Ar), 7.20-7.30 (m, 5H, Ar-H). ^{13}C NMR (CDCl_3) δ : –5.2 ($\text{Si}(\text{CH}_3)_2$), 18.1 ($\text{Si}(\text{CH}_3)_3$), 25.8 ($\text{Si}(\text{CH}_3)_3$), 51.1 (NCH_2), 59.1 (CHCH_2O), 61.4 and 63.0 (CH_2OH and CH_2OSi), 126.9, 127.9, 128.4 and 140.2 (Ar). MS, m/z (%) = 296 (100) [M^+]. Anal. calc. for $\text{C}_{16}\text{H}_{29}\text{NO}_2\text{Si}$: C, 65.03; H, 9.89, N, 4.74, found: C, 64.75; H, 9.85, N, 4.55.

(2S)-2-[N-Benzyl-N-[(E)-(3-methyl-4-triethyloxy)-2-butenyl]-amino]-3-tert-butylidimethylsilyloxy-1-propanol (5) To a suspension of NaHCO₃ (6.61 g, 78.67 mmol) in CH₃CN (40 ml) at room temperature was added over 5 min a solution of **4** (9.29 g, 31.47 mmol) in CH₃CN (25 ml). The reaction mixture was stirred for additional 30 min at room temperature. Freshly prepared alkenyl bromide **21** (10.76 g, 38.69 mmol) in CH₃CN (30 ml) was added and the mixture was refluxed for 3 h. The reaction mixture was quenched with saturated NH₄Cl (8 ml) and the aqueous phase extracted with AcOEt (3x80 ml). The combined organic phases were washed with brine, dried (MgSO₄), and concentrated *in vacuo*. The crude product was purified by flash chromatography, R_f 0.42 (1:1 Et₂O-PE) affording **5** (12.73 g, 82%) as a colourless oil. $[\alpha]_D^{20} = -3.6$ (c 0.91, CHCl₃). IR (film): $\nu/\text{cm}^{-1} = 3343\text{--}3553$ (OH), 2916, 1441, 1238. ¹H NMR (CDCl₃, 400 Mz) δ : 0.03 (s, 6H, Si(CH₃)₂), 0.55 (q, 6H, Si(CH₂CH₃)₃), 0.81 (s, 9H, SiC(CH₃)₃), 0.90 (t, 9H, J = 7.3 Hz, Si(CH₂CH₃)₃), 1.49 (s, 3H, -CH=C(CH₃)), 2.92 (m, 1H, CHCH₂OH), 3.18 (m, 2H, NCH₂CH=C-), 3.37 (dd, 1H, J = 3.7, 10.1 Hz, CH₂OH), 3.51 (m, 3H, CH₂OSi and CH₂OH), 3.60 (d, 1H, J = 7.2 Hz, NCH₂Ar), 3.81 (d, 1H, J = 7.2 Hz, NCH₂Ar), 3.91 (s, 2H, CH₂OSi(CH₂CH₃)₃), 5.41 (t, 1H, J = 6.1 Hz, NCH₂CH=C), 7.11–7.20 (m, 5H, ArH). ¹³C NMR (CDCl₃) δ : -5.2 (Si(CH₃)₂), 4.9 (Si(CH₂CH₃)₃), 7.15 (Si(CH₂CH₃)₃), 14.1 (-CH=C(CH₃)), 18.5 (SiC(CH₃)₃), 26.4 (SiC(CH₃)₃), 47.4 (NCH₂CH=C-), 54.6 (CH₂OSi), 59.8 (NCH₂), 60.0 (CHCH₂OH), 61.2 (CHCH₂OH), 68.4 (CH₂OSi), 122.9 (NCH₂CH=C), 127.3, 128.7, 129.2, 137.9 and 140.3 (NCH₂CH=C- and Ar). MS, *m/z* (%) = 493 (0.5) [M⁺]; 478 (2) [M-CH₃⁺]; 462 (66) [M-H-CH₃x2⁺]; 348 (100) [M-OTES⁺]. Anal. calc. for C₂₇H₅₁NO₃Si₂: C, 65.66; H, 10.41, N, 2.84, found: C, 65.63; H, 10.52, N, 2.72.

(2E,4S)-4-[N-Benzyl-N-[(E)-(3-methyl-4-triethylsilyloxy)-2-butenyl]-amino]-5-(tert-butylidimethylsilyloxy)-2-pentenoic acid ethyl ester (6) A solution of dimethyl sulfoxide (1.19 ml, 16.77 mmol) in dichloromethane (6 ml) was added to a solution of oxalyl chloride (0.67 ml, 7.74 mmol) in dichloromethane (15 ml) at -78 °C, and the reaction mixture was stirred for 5 more min at the same temperature. A solution of the alcohol (**5**) (3.18 g, 6.32 mmol) in dichloromethane (15 ml) was added over 5 min and stirring was continued for another 20 min after which NEt₃ (4.53 ml, 32.26 mmol) was added and the solution brought to -15 °C over 2 h. A solution of methyl (triphenylphosphoranylidene)acetate (6.65 g, 18.71 mmol) in dichloromethane (15 ml) was added to the reaction mixture and the temperature was allowed to reach at 25 °C over 3 h. The reaction mixture was poured into brine (30 ml) and the solution was extracted with dichloromethane (3x50 ml). The combined organic phases were dried (MgSO₄), and concentrated *in vacuo*. The crude product was purified by flash chromatography, R_f 0.58 (5:95 Et₂O-PE) affording **6** (5.43 g, 75%) as a pale yellow oil. $[\alpha]_D^{20} +8.2$ (c 1.59, CHCl₃). IR (film): $\nu/\text{cm}^{-1} = 2833\text{--}2930$, 1693 (C=O), 1441, 1246. ¹H NMR (CDCl₃, 400 Mz) δ : 0.04 (s, 6H, Si(CH₃)₂), 0.55 (q, 6H, Si(CH₂CH₃)₃), 0.86 (s, 9H, SiC(CH₃)₃), 0.92 (t, 9H, J = 7.1 Hz, Si(CH₂CH₃)₃), 1.26 (t, 3H, J = 7.2 Hz, CO₂CH₂CH₃), 1.52 (s, 3H, -CH=C(CH₃)), 3.11 (m, 1H, NCH₂CH=C-), 3.21 (m, 1H, NCH₂CH=C-), 3.40 (m, 1H, CHCH=CH), 3.62 (d, 1H, J = 7.2 Hz, NCH₂Ar), 3.79–3.88 (m, 3H, CH₂OSi(CH₃)₂ and NCH₂Ar), 4.11 (s, 2H, CH₂OSi(CH₂CH₃)₃), 4.21 (q, 2H, J = 7.1, 14.1 Hz, CO₂CH₂CH₃), 5.55 (t, 1H, J = 7.5 Hz, NCH₂CH=C-), 6.05 (d, 1H, J = 15.1 Hz, CH=CHCO₂Et), 7.03 (CH=CHCO₂Et), 7.21–7.35 (m, 5H, ArH). ¹³C NMR (CDCl₃) δ : -5.1 (Si(CH₃)₂), 4.9 (Si(CH₂CH₃)₃), 7.2 (Si(CH₂CH₃)₃), 14.1 (-CH=C(CH₃)), 14.6 (CO₂CH₂CH₃), 18.6 (SiC(CH₃)₃), 26.2 (SiC(CH₃)₃), 48.2 (NCH₂CH=C-), 55.3 (CH₂N), 60.6 (CO₂CH₂CH₃), 61.9 (CHCH=CH), 63.9 and 68.4 (CH₂OSi), 123.2 (NCH₂CH=C-), 123.9 (CH=CHCO₂Et), 127.1, 128.5, 128.8, 137.6 and 140.6 (NCH₂CH=C- and Ar), 147.1 (CH=CHCO₂Et), 166.8 (C=O). MS, *m/z* (%) = 561 (3) [M⁺]; 532 (4) [M-CH₂CH₃⁺];

416 (100) [M-2xCH₃-OTES⁺]. Anal. calc. for C₃₁H₅₅NO₄Si₂: C, 66.26; H, 9.87, N, 2.49, found: C, 65.90; H, 10.04, N, 2.35.

(2E,4S)-4-[N-Benzyl-N-[(2E)-(4-hydroxy-3-methyl-4-hydroxy)-2-butenyl]-amino]-5-(tert-butyldimethylsilyloxy)-2-pentenoic acid ethyl ester (7) A 1 M solution of tetrabutylammonium fluoride (TBAF) (3.02 ml, 3.02 mmol) in THF (10 ml) was added with stirring at 0 °C to a solution of **6** (1.54 g, 2.74 mmol) in THF (10 ml). The reaction mixture was stirred an additional 5 min, diluted with H₂O (10 ml) and extracted with Et₂O (3x20 ml). The combined organic phases were dried (MgSO₄) and evaporated to dryness. The residue was purified by a flash chromatography, R_f 0.35 (1:1 AcOEt-PE) on a short column affording **7** (0.98 g, 81%) as a pale yellow oil. [α]_D²⁰ +14.7 (c 0.61, CHCl₃). IR (film): ν /cm⁻¹ = 3318-3526 (OH), 1721 (C=O), 1650, 1470, 1369. ¹H NMR (CDCl₃, 400 Mz) δ : 0.04 (s, 6H, Si(CH₃)₂), 0.86 (s, 9H, SiC(CH₃)₃), 1.29 (t, 3H, J = 7.4 Hz, CO₂CH₂CH₃), 1.59 (s, 3H, -CH=C(CH₃)), 3.19 (m, 2H, NCH₂CH=C-), 3.40 (m, 1H, CHCH=CH), 3.60 (d, 1H, J = 7.1 Hz, NCH₂Ar), 3.70-3.82 (m, 3H, CH₂OSi and NCH₂Ar), 3.91 (s, 2H, CH₂OH), 4.19 (q, 2H, J = 7.5, 14.8 Hz, CO₂CH₂CH₃), 5.45 (t, 1H, J = 7.3 Hz, NCH₂CH=C-), 5.98 (d, 1H, J = 14.9 Hz, CH=CHCO₂Et), 6.98 (dd, 1H, J = 15.7 Hz, CH=CHCO₂Et), 7.19-7.31 (m, 5H, ArH). ¹³C NMR (CDCl₃) δ : -3.7 (Si(CH₃)₂), 13.8 (-CH=C(CH₃)), 14.2 (CO₂CH₂CH₃), 18.1 (SiC(CH₃)₃), 25.7 (SiC(CH₃)₃), 48.0 (NCH₂CH=C-), 55.3 (NCH₂Ar), 60.2 (CO₂CH₂CH₃), 61.9 (CHCH=CH), 63.4 and 68.4 (CH₂OSi and CH₂O), 123.3 (NCH₂CH=C-), 124.2 (CH=CHCO₂Et), 126.7, 128.1, 128.3, 137.0 and 140.2 (NCH₂CH=C- and Ar), 146.6 (CH=CHCO₂Et), 166.4 (C=O). HRMS (*m/z*) for C₂₅H₄₁NO₄Si [(M+Na)⁺] calc. 448.2840, found: 448.2883.

(2E,4S)-4-[N-Benzyl-N-[(2E)-(4-chloro-3-methyl-4-hydroxy)-2-butenyl]-amino]-5-(tert-butyldimethylsilyloxy)-2-pentenoic acid ethyl ester (8) To a solution of **7** (3.77 g, 8.43 mmol) in dichloromethane (30 ml) were added NEt₃ (1.89 ml, 13.49 mmol) and methanesulfonyl chloride (0.85 ml, 10.96 mmol) at -40 °C under argon atmosphere. After being stirred at the same temperature for 1 h, the reaction mixture was injected to a suspension of dry LiCl (1.43 g, 33.72 mmol) in THF (10 ml) and the reaction mixture was allowed to room temperature overnight. The reaction mixture was poured into pentane (30 ml) and washed with H₂O several times. The organic phase was dried (MgSO₄), and concentrated *in vacuo*. The crude product was purified by flash chromatography, R_f 0.48 (5:95 Et₂O-PE) affording **8** (2.79 g, 71%) as a colourless oil. [α]_D²⁰ +22.0 (c 0.78, CHCl₃). IR (film): ν /cm⁻¹ = 2956-2857, 1686 (s, C=O), 1426. ¹H NMR (CDCl₃, 300 Mz) δ : 0.03 (s, 6H, Si(CH₃)₂), 0.84 (s, 9H, SiC(CH₃)₃), 1.26 (t, 3H, J = 8.5 Hz, CO₂CH₂CH₃), 1.67 (s, 3H, -CH=C(CH₃)), 3.12 (dd, 1H, J = 14.7 Hz, NCH₂CH=C-), 3.24 (dd, 1H, J = 14.4 Hz, NCH₂CH=C-), 3.37 (m, 1H, CHCH=CH), 3.59 (d, 1H, J = 14.0 Hz, NCH₂Ar), 3.69-3.83 (m, 3H, CH₂OSi and NCH₂Ar), 3.94 (s, 2H, CH₂Cl), 4.18 (q, 2H, J = 7.0, 15.0 Hz, CO₂CH₂CH₃), 5.61 (t, 1H, J = 6.0 Hz, NCH₂CH=C-), 5.97 (d, 1H, J = 16.3 Hz, CH=CHCO₂Et), 6.92 (dd, 1H, J = 16.7 Hz, CH=CHCO₂Et), 7.18-7.32 (m, 5H, ArH). ¹³C NMR (CDCl₃) δ : -3.0 (Si(CH₃)₂), 16.7 (-CH=C(CH₃)), 16.9 (CH₂CH₃), 20.6 (SiC(CH₃)₃), 28.2 (SiC(CH₃)₃), 50.6 (NCH₂CH=C-), 54.2 (NCH₂Ar), 57.6 (CO₂CH₂CH₃), 62.7 (CH₂Cl), 64.2 (CHCH=CH), 65.9 (CH₂OSi), 126.1 (NCH₂CH=C-), 129.3 (CH=CHCO₂Et), 130.6, 130.8, 131.6, 136.4 and 142.3 (NCH₂CH=C- and Ar), 148.7 (CH=CHCO₂Et), 168.7 (C=O). HRMS (*m/z*) for C₂₅H₄₀ClNO₃Si [(M+H)⁺] calc. 446.2551, found: 446.2544.

(2E,4S)-4-[N-Benzyl-N-[(2E)-(4-chloro-3-methyl)-2-butenyl]amino]-5-(tert-butyldimethylsilyloxy)-2-penten-1-ol (11) To a solution of DIBAL-H (1M in hexane) (7.98 ml, 7.98 mmol) in dichloromethane (20 ml) at

–78 °C was added dropwise a solution of ester **10** (1.24 g, 2.66 mmol) in dichloromethane (15 ml) under a nitrogen atmosphere. After being stirred at the same temperature for 2 h, a solution of AcOH (1M in dichloromethane) (5 ml) was added and the reaction mixture was poured into a funnel containing a 10% solution of tartaric acid (30 ml), extracted with dichloromethane (3x40 ml), dried (MgSO₄) and concentrated under reduced pressure. The crude product was purified by flash chromatography, R_f 0.27 (4:6 Et₂O-PE) affording **11** (0.80 g, 70%) as a colourless oil. $[\alpha]_D^{20} +7.2$ (c 0.76, CHCl₃). IR (film): ν/cm^{-1} = 3226-3491 (OH), 2956-2856, 1461, 1426. ¹H NMR (CDCl₃, 400 Mz) δ : 0.00 (s, 6H, Si(CH₃)₂), 0.85 (s, 9H, SiC(CH₃)₃), 1.66 (s, 3H, –CH=C(CH₃)), 3.05-3.26 (m, 3H, NCH₂CH=C– and CHCH=CH), 3.53 (d, 1H, *J* = 13.4 Hz, NCH₂Ar), 3.64-3.78 (m, 3H, CH₂OSi and NCH₂Ar), 3.94 (s, 2H, CH₂Cl), 4.14 (m, 2H, CH₂OH), 5.57 (t, 1H, *J* = 6.8 Hz, NCH₂CH=C–), 5.64-5.81 (m, 2H, CH=CHCH₂OH), 7.15-7.33 (m, 5H, ArH). ¹³C NMR (CDCl₃) δ : –4.6 (Si(CH₃)₂), 14.4 (–CH=C(CH₃)), 18.1 (SiC(CH₃)₃), 25.8 (SiC(CH₃)₃), 48.1 (NCH₂CH=C–), 51.4 (CH₂Cl), 54.9 (NCH₂Ar), 62.3 (CHCH=CH), 63.4 (CH₂OH), 64.1 (CH₂OSi), 126.6 (NCH₂CH=C–), 126.9 (CH=CHCH₂OH), 128.0, 128.4, 128.7, 129.6 and 132.7 (NCH₂CH=C– and Ar), 133.3 (CH=CHCH₂OH). MS, *m/z* (%) = 423 (100) [M⁺]; 389 (8) [M–HCl⁺]. Anal. calc. for C₂₃H₃₈ClNO₂Si: C, 65.14; H, 9.03, N, 3.30, found: C, 64.85; H, 9.34, N, 2.99.

(2E,4S)-4-[N-Benzyl-N-[(2E)-(4-chloro-3-methyl)-2-butenyl]-amino]-5-(tert-butyldimethylsilyloxy)-2-penten-1-yl N,N-diisopropylcarbamate (12) To a suspension of sodium hydride (60% suspension mineral oil) (0.18 g, 4.60 mmol) in THF (5 ml) was added over 10 min a solution of **11** (1.30 g, 3.07 mmol) in THF (15 ml). The reaction mixture was stirred at room temperature for 1 h, after which time a solution of *CbCl* (1.50 g, 9.21 mmol) in THF (15 ml) was added and the reaction mixture was heated to 70 °C for 12 h. The reaction mixture was allowed to chill to room temperature and treated with saturated NH₄Cl (10 ml) and H₂O (10 ml). The phases were separated and the aqueous phase was extracted with ether (3x25 ml). The combined organic phases were dried (MgSO₄), and concentrated *in vacuo*. The crude product was purified by flash chromatography, R_f 0.44 (2:8 Et₂O-PE) affording **12** (0.89 g, 53%) as a colourless oil. $[\alpha]_D^{20} +9.7$ (c 0.71, CHCl₃). IR (film): ν/cm^{-1} = 2952-2852, 1721 (NC=O), 1586, 1469, 1365. ¹H NMR (CDCl₃, 400 Mz) δ : 0.03 (s, 6H, Si(CH₃)₂), 0.90 (s, 9H, SiC(CH₃)₃), 1.19 (s, 6H, CH₃–*Cb*), 1.21 (s, 6H, CH₃–*Cb*), 1.70 (s, 3H, CH=C(CH₃)), 3.09-3.28 (m, 2H, NCH₂CH=C), 3.29 (m, 1H, CHCH=CH), 3.50 (d, 1H, *J* = 13.0 Hz, NCH₂Ar), 3.68-3.80 (m, 4H, NCH₂Ar, CH₂OSi and CH–OC*b*), 3.97 (br s, 3H, CH₂Cl and CH–OC*b*), 4.60 (s, 2H, CH₂OC*b*), 5.69 (t, 1H, *J* = 6.1 Hz, NCH₂CH=C–), 5.69-5.80 (m, 2H, –CH=CHCH₂OC*b*), 7.26-7.48 (m, 5H, ArH). ¹³C NMR (CDCl₃) δ : –5.2 (Si(CH₃)₂), 14.3 (–CH=C(CH₃)), 18.1 (SiC(CH₃)₃), 21.0 (CH₃–*Cb*), 25.8 (SiC(CH₃)₃), 28.7 (CH–*Cb*), 48.1 (NCH₂CH=C–), 51.9 (CH₂Cl), 54.9 (NCH₂Ar), 62.3 (CHCH=CH), 64.6 (CH₂OSi), 64.8 (CH₂OC*b*), 126.6, 128.0, and 128.4 (Ar), and 128.9 (CH=CHCH₂OC*b*), 129.6 (NCH₂CH=C–), 130.8 (CH=CHCH₂OC*b*), 133.3 and 140.3 (NCH₂CH=C– and Ar), 155.3 (NC=O). MS, *m/z* (%) = 551 (100) [M⁺]. Anal. calc. for C₃₀H₅₁ClN₂O₃Si: C, 65.36; H, 9.32, N, 5.08, found: C, 65.38; H, 9.35, N, 4.89.

[2R,3S,3(1Z),4S]-1-Benzyl-2-[(tert-butyldimethylsilyloxy)methyl]-3-[2-(N,N-diisopropylcarbamoyloxy)-ethenyl]-4-(1-methyletenyl)-pyrrolidine (13a) The chloride **12** (0.116 g, 0.211 mmol) and (–)-sparteine (0.114 g, 0.485 mmol) were dissolved in toluene (10 ml) and cooled to –78 °C. After slow addition of *n*-BuLi (1.6 M in hexane) (0.30 ml, 0.485 mmol), the solution was stirred for 90 min. MeOH (1 ml) and NH₄Cl (0.5 ml) were added, and the reaction mixture was allowed to warm to room temperature. The organic layer was separated and the aqueous phase was extracted with Et₂O (3x10 ml). The combined organic phases were dried (MgSO₄),

and concentrated *in vacuo*. The crude was purified by flash chromatography, R_f 0.48 and 0.33 (20:80 Et₂O-PE) affording **13a** and **13b**, respectively (0.089 g, 83%, *d.r.* = 80:20) as a colourless oil. **13a**: $[\alpha]_D^{20} = -22.6$ (c 0.57, CHCl₃). IR (film): $\nu/\text{cm}^{-1} = 2960\text{--}2852$, 1713 (NC=O), 1465, 1430, 1365. ¹H NMR (CDCl₃, 600 Mz) δ : 0.01 (s, 6H, Si(CH₃)₂), 0.86 (s, 9H, SiC(CH₃)₃), 1.23–1.25 (m, 12H, CH₃-Cb), 1.62 (s, 3H, CH=C(CH₃)), 2.46–2.50 (m, 1H, CH₂N), 2.57 (dd, 1H, *J* = 9.8 Hz, CHCH₂OSi), 2.81–2.85 (m, 1H, CHC(CH₃)=CH₂), 2.95 (d, 1H, *J* = 8.7 Hz, CH₂N), 3.17–3.21 (m, 1H, CHCH=CHOCb), 3.46 (d, 1H, *J* = 13.2 Hz, NCH₂Ar), 3.61–3.63 (m, 2H, CHCH₂OSi), 3.89 (br s, 1H, CHOCb), 3.98 (br s, 1H, CHOCb), 4.19 (d, 1H, *J* = 13.4 Hz, NCH₂Ar), 4.53 (br s, 1H, CHC(CH₃)=CH₂), 4.60 (dd, 1H, *J* = 11.9 Hz, CH=CHOCb), 4.71 (br s, 1H, CHC(CH₃)=CH₂), 6.97 (d, 1H, *J* = 5.6 Hz, CH=CHOCb), 7.22–7.35 (m, 5H, ArH). ¹³C NMR (CDCl₃) δ : –5.4 (Si(CH₃)₂), 19.1 (SiC(CH₃)₃), 20.6, 21.3 (CH₃-OCb), 22.9 (CH=C(CH₃)), 25.9 (SiC(CH₃)₃), 27.9 (CH-OCb), 39.4 (CHCH=CHOCb), 47.0 (CHC(CH₃)=CH₂), 56.1 (NCH₂), 60.4 (NCH₂Ar), 66.6 (CH₂OSi), 72.4 (CHCH₂OSi), 110.1 (CHC(CH₃)=CH₂), 111.0 (CH=CHOCb), 126.7, 128.1 and 128.8 (Ar), 134.4 (CH=CHOCb), 139.8 (Ar), 143.9 (CHC(CH₃)=CH₂), 153.6 (NC=O). HRMS (*m/z*) for C₃₀H₅₀N₂O₃Si [(M+H)⁺] calc. 515.3658, found: 515.3669.

[2R,3S,3(1E),4S]-2-(tert-butylidimethylsilyloxy)methyl-3-[2-(N,N-diisopropylcarbamoyloxy)-2-methylthioethenyl]-4-(1-methyletenyl)-pyrrolidine-1-carboxylic acid methyl ester (16a) To a solution pre-cooled to –78 °C of **13a** (0.110 g, 0.214 mmol) and TMEDA (0.052 g, 0.449 mmol) in THF (10 ml), a solution of *t*-BuLi (1.7 M in pentane) (0.298 ml, 0.449 mmol) was added dropwise. The resulted solution was stirred for 1 h at –78 °C. It was then quenched with MeSSMe (0.192 ml, 2.14 mmol) and the resulting mixture was allowed to warm to room temperature. The aqueous phase was extracted with Et₂O (3x10 ml). The combined organic phases were washed with brine, dried (MgSO₄), and concentrated *in vacuo* affording the crude product **15a** as a yellow oil which was used in the next step without further purification. To a solution of crude product **15a** in dry 1,2-dichloroethane (10 ml), methoxy chloroformate (0.083 ml, 1.07 mmol) was added dropwise at room temperature. The resulted solution was refluxed for 3 h, after that, the solvent was evaporated *in vacuo*. The crude product was purified by flash chromatography, R_f 0.48 (1:1 Et₂O-PE) affording **16a** (0.095 g, 84%). $[\alpha]_D^{20} = -19.0$ (c 0.57, CHCl₃). IR (film): $\nu/\text{cm}^{-1} = 2952\text{--}2856$, 1708 (NC=O), 1447, 1382. ¹H NMR (CDCl₃, 400 Mz) δ : 0.00 (s, 6H, Si(CH₃)₂), 0.89 (s, 9H, SiC(CH₃)₃), 1.20–1.23 (m, 12H, CH₃-Cb), 1.50 (s, 3H, CH=C(CH₃)), 2.20 (s, 3H, SMe), 2.40–2.45 (m, 1H, CHCH₂OSi), 3.32–3.40 (m, 2H, CHCH=C(SMe)OCb and NCH₂), 3.61 (s, 3H, NCO₂Me), 3.65 (m, 2H, NCH₂, CHC(CH₃)=CH₂), 3.85 (m, 2H, CH₂OSi), 3.88–3.99 (br s, 2H, CHOCb), 4.60 (br s, 1H, CHC(CH₃)=CH₂), 4.80 (br s, 1H, CHC(CH₃)=CH₂), 5.55 (d, 1H, *J* = 10.3 Hz, CH=C(SMe)OCb). HRMS (*m/z*) for C₂₆H₂₈N₂O₅SSi [(M+H)⁺] calc. 529.310321, found: 529.312596.

(2S,3S,4S)-2-(hydroxymethyl)-3-[2-(methoxycarbonyl)-ethyl]-4-(1-methyletenyl)-pyrrolidine-1-carboxylic acid methyl ester (17a) To a solution of **16a** (0.109 g, 0.206 mmol) in MeOH (10 ml), methanesulfonic acid (0.054 ml, 0.825 mmol) and 3 drops of water were added. The reaction mixture was refluxed for 16 h. The mixture was diluted with H₂O and the aqueous phase was extracted with ether (3x10 ml). The organic phase was washed with saturated NaHCO₃, dried (MgSO₄), and concentrated *in vacuo*. The crude product was purified by flash chromatography, R_f 0.39 (70:30 AcOEt-Et₂O) affording **17a** (0.31 g, 55%) as a colourless oil which was identical spectroscopically (NMR) to the product obtained by Chevliakov et al.⁴ⁱ $[\alpha]_D^{20} = -41.0$ (c 0.39, CH₂Cl₂). Lit.⁴ⁱ $[\alpha]_D^{20} = -43.0$ (c 1.25, CH₂Cl₂). HRMS (*m/z*) for C₁₃H₂₁NO₅ [(M+Na)⁺] calc. 294.131194, found: 294.130890.

(–)- α -kainic acid (1) Deprotection of kainic acid was carried out by the method of Chevliakov.⁴ⁱ The final compound was identical spectroscopically (NMR). mp 243–245 °C (decomp); Lit.⁴ⁱ 241–244 °C (decomp). $[\alpha]_D^{20}$ –14.3 (c 0.40, H₂O). Lit.⁴ⁱ $[\alpha]_D^{20}$ –14.6 (c 0.25, H₂O). HRMS (m/z) for C₁₀H₁₅NO₄ [(M–H)⁺] calc. 212.0928, found: 212.0920.

(3*R*,3*aR*,7*aS*)-3-(1-methylethenyl)-5-oxooctahydropyrano-[3,4*b*]pyrrole-1-carboxylic acid methyl ester (18*b*) To a solution of **18b** (0.032 g, 0.060 mmol) in MeOH (8 ml), methanesulfonic acid (0.015 ml, 0.242 mmol) and 2 drops of water were added. The reaction mixture was refluxed for 15 h. The mixture was diluted with H₂O and the aqueous phase was extracted with ether. The organic phase was washed with saturated NaHCO₃, dried (MgSO₄), and concentrated *in vacuo*. The crude was purified by flash chromatography R_f 0.20 (1:2 EE-petroleum ether) affording **18b** (0.007 g, 48%) as a colourless oil which was identical spectroscopically (NMR) to the product obtained by Campbell et al.^{4j} $[\alpha]_D^{20}$ –28.1 (c 0.30, CHCl₃). Lit.^{4j} (*ent*-**18b**.) $[\alpha]_D^{20}$ +32.1 (c 1.20, CH₂Cl₂). HRMS (m/z) for C₁₂H₁₈NO₄ [(M+H)⁺] calc. 240.1230, found: 240.1221.

ARX300, CDCl₃,

USER: -- DATE: Sat Jan 24 00:31:46 2004

F1: 300.135

SW1: 3906

OF1: 1673.7

PTS1d: 16284

EX: zg30

PW: 10.0 usec

PD: 0.1 sec

NA: 40

LB: 0.0

WinNuts - \$

(-)-13a