Stereoselective Synthesis of the Bioactive Polypropionates Aureothin, *N*-Acetylaureothamine and Aureonitrile

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Supporting Information

General. Unless otherwise noted, infrared spectra (IR) were obtained on NaCl plates with a ATI Mattson Gemini FTIR spectrometer. High-resolution mass spectra (HRMS) were obtained on VG ProSpec Mass Spectrometer using electron impact (EI) at 70 eV unless otherwise noted

All reaction mixtures were magnetically stirred in oven-dried glassware under a blanket of nitrogen. External bath temperatures were used to record all reaction mixture temperatures. Analytical thin layer chromatography (TLC) was carried out on Merck silica gel 60 F₂₅₄ TLC plates. TLC visualization was accomplished using 254 nm UV light or charring solutions of KMnO₄. Flash chromatography was performed on ICN siliTech 32-63 D 60 Å silica gel according to the procedure of Still.¹

Tetrahydrofuran (THF), dichloromethane (CH₂Cl₂) were dried according to the procedure described by Bergman.² Benzene was distilled from CaH₂ immediately prior to use. DMF was dried over 4 Å molecular sieves. Extracts were dried over anhydrous MgSO₄ and solvents were removed with a rotary evaporator at aspirator pressure.

The intermediates which are not shown in the paper are numbered as following:

In the cases where same types of reactions were involved, a representative procedure was demonstrated.

2-Iodomethyl-4-iodomethylene-tetrahydro-furan (**6**)

To a mixture of (Z)-iodoallylic alcohol **5** (2.05 g, 9.20 mmol), NaHCO₃ (40.0g, 471 mmol) and 3 Å m.s. in dry MeCN (800 mL) at 0 °C was slowly added a solution of I₂ (6.94 g, 27.3 mmol) in dry MeCN(200 mL). The reaction mixture was stirred violently at 0 °C for 1 h and then was allowed to warm to r.t. The reaction mixture was filtered through a pad of Celite and the organic solution was washed with Saturated Na₂S₂O₃ aqueous solution (200 mL). The aqueous layer was washed with ether (2 X 300 mL) and the combined organic layers were washed with brine (300 mL), dried, filtered and concentrated *in vacuo*. The product was purified by column chromatography (EtOAc: hexanes = 1:20) to afford 3.10 g (97%) of **6** as colorless oil. R_f 0.44 (EtOAc: hexanes = 1:20); IR 3064, 2890, 2843, 1642cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ_H 6.00 (t, 1 H, *J* = 2.0 Hz), 4.38 (d, 1 H, *J* = 14.6 Hz), 4.21 (d, 1 H, *J* = 14.6 Hz), 4.17 (m, 1 H), 3.26-3.17 (m, 2 H), 2.78 (dd, 1 H, *J* = 15.9, 6.0 Hz), 2.42 (dd, 1 H, *J* = 15.9, 7.4 Hz); ¹³C NMR (100 MHz, CDCl₃) δ_C 150.05, 80.14, 75.86, 67.87, 40.82, 8.24; HRMS calcd for C₆H₈I₂O (M)⁺ 349.8665, found: 349.8667

(4-Iodomethylene-tetrahydro-furan-2-yl)-methanol (**7**)

A mixture of CF₃CO₂Cs (1.75 g, 7.11 mmol) and 3 Å m. s.(0.50 g) and **6** (0.50 g, 1.43 mmol) in dry DMF (16 mL) was stirred at 90 °C for 44 h. The reaction mixture was filtered through a pad of Celite into a NaOH solution (1 N, 200 mL) at 0 °C. The reaction flask and the Celite were rinsed with EtOAc (300 mL). The two layered were separated and the aqueous layer was washed with EtOAc (100 mL). The combined organic layers were washed with brine (50 mL), dried, filtered and concentrated *in vacuo*. The product was purified by column chromatography (EtOAc: hexanes = 1:2) to afford 0.285 g (83%) of **7** as colorless oil. R_f 0.40 (EtOAc: hexanes = 1:2); IR 3390(br), 3063, 2924, 2866, 1663cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ_H 5.98 (t, 1 H, *J* = 2.2 Hz), 4.35 (d, 1 H, *J* = 14.5 Hz), 4.25-4.16 (m, 2 H), 3.71 (m, 1 H), 3.55 (m, 1 H), 2.60 (dd, 1 H, *J* = 15.9, 6.3 Hz), 2.47 (dd, 1 H, *J* = 15.9, 8.6 Hz), 2.22 (t, 1 H, *J* = 6.2 Hz); ¹³C NMR (100 MHz, CDCl₃) δ_C 150.83, 81.31, 75.52, 66.96 63.78, 35.96; HRMS calcd for C₆H₉IO₂ (M)⁺ 239.9647, found: 239.9652

8

tert-Butyl-(4-iodomethylene-tetrahydro-furan-2-ylmethoxy)-diphenyl-silane (8)

To a mixture of imidazole (0.766 g, 11.3 mmol) and **7** (0.45 g, 1.88 mmol) in DMF (5 mL) was added TBDPSCl (1.55 g, 5.63 mmol). The reaction mixture was stirred for 1 h and then quenched with water (50 mL). The mixture was extracted with EtOAc (3 X 50 mL) and the combined organic layers were washed with brine (30 mL), dried, filtered and concentrated *in vacuo*. The product was purified by column chromatography (EtOAc: hexanes = 1:30) to afford 0.852 g (95%) of **8** as colorless oil. R_f 0.45 (EtOAc: hexanes = 1:20); IR 3070, 3048, 2929, 2856, 2361, 2337 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ_{H} 7.71-7.66 (m, 4 H), 7.45-7.37 (m, 6 H), 5.96 (m, 1 H), 4.38 (d, 1 H, J = 14.5 Hz), 4.31 (m, 1 H), 4.25 (m, 1 H), 3.72 (d, 2 H, J = 4.6 Hz), 2.72-2.65 (m, 1 H), 2.61-2.53 (m, 1 H), 1.08 (s, 9 H); ^{13}C NMR (100 MHz, CDCl_3) δ_{C} 151.52, 135.66, 133.42, 129.78, 127.78, 81.28, 75.88, 66.29, 66.00, 36.95, 26.90, 19.32

S-1

2-(tert-Butyl-diphenyl-silanyloxymethyl)-4-(3-trimethylsilanyl-prop-2-ynylidene)-tetrahydro-furan (S-1)

A mixture of **8** (0.760 g, 1.59 mmol), TMSA (0.466 g, 4.76 mmol), $\text{Pd}(\text{PPh}_3)_2\text{Cl}_2$ (0.112 g, 0.159 mmol), CuI (0.060 g, 0.32 mmol) in THF (10 mL) and NEt_3 (10 mL) was heated at 70 °C for 5 h. The reaction mixture was cooled to r.t. and was then diluted with EtOAc (100 mL) and the mixture was filtered through a pad of Celite. The reaction flask and the Celite were rinsed with EtOAc (50 mL) and the combined organic filtrates were washed with brine (30 mL), dried, filtered and concentrated *in vacuo*. The product was purified by column chromatography (EtOAc: hexanes = 1:30) to afford 0.685 g (96%) of **S-1** as colorless oil. R_f 0.34 (EtOAc: hexanes = 1:20); IR 3071, 3049, 2957, 2930, 2897, 2858, 2168, 2121 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ_{H} 7.71-7.66 (m, 4 H), 7.45-7.37 (m, 6 H), 5.49 (t, 1 H, J = 2.4 Hz), 4.63 (d, 1 H, J = 15.2 Hz), 4.49 (d, 1 H, J = 15.2 Hz), 4.20 (m, 1 H), 3.72 (d, 2 H, J = 4.6 Hz), 2.75-2.69 (m, 1 H), 2.64-2.58 (m, 1 H), 1.08 (s, 9 H), 0.20 (s, 9 H); ^{13}C NMR (100 MHz, CDCl_3) δ_{C} 156.62, 135.61, 135.60, 133.43, 133.39, 129.70, 129.67, 127.70, 101.79, 99.89, 98.60, 79.97, 71.32, 65.83, 35.02, 26.80, 19.24, 0.04

9

tert-Butyl-[4-(2-methyl-allylidene)-tetrahydro-furan-2-ylmethoxy]-diphenyl-silane (9)

To a mixture of **S-1** (0.720 g, 1.61 mmol) in MeOH (12 mL) and CH₂Cl₂ (12 mL) was added K₂CO₃ (3.33 g, 24.2 mmol) at 0°C. The reaction mixture was allowed to warm to r.t. and was stirred for 2 h. The reaction mixture was then partitioned between water (50 mL) and CH₂Cl₂ (100 mL). The aqueous layer was washed with CH₂Cl₂ (2 X 30 mL) and the combined organic layers were washed with brine (40 mL), dried, filtered and concentrated *in vacuo*. The product was purified by column chromatography (EtOAc: hexanes = 1:20) to afford 0.600 g (99%) of **9** as colorless oil. *R*_f 0.28 (EtOAc: hexanes = 1:20); IR 3305, 3289, 3071, 2930, 2857 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ_H 7.76-7.73 (m, 4 H), 7.49-7.41 (m, 6 H), 5.48 (m, 1 H, *J* = 2.4 Hz), 4.69 (d, 1 H, *J* = 15.2 Hz), 4.55 (d, 1 H, *J* = 15.2 Hz), 4.25 (m, 1 H), 3.79 (d, 2 H, *J* = 4.6 Hz), 3.12 (s, 1 H), 2.76 (dd, 1 H, *J* = 16.8, 6.8 Hz), 2.66 (dd, 1 H, *J* = 16.8, 6.8 Hz), 1.13 (s, 9 H); ¹³C NMR (100 MHz, CDCl₃) δ_C 157.17, 135.65, 133.45, 133.43, 129.78, 127.76, 127.78, 98.81, 81.46, 80.35, 80.00, 71.30, 65.92, 35.03, 26.88, 19.30

10

tert-Butyl-[4-(2-methyl-3-tributylstannanyl-allylidene)-tetrahydro-furan-2-ylmethoxy]-diphenyl-silane (10)

To a SnCl₂ (1.88 g, 9.90 mmol) suspension in THF (25 mL) at 0 °C was added nBuLi (12.8 mL, 28.8 mmol, 2.25 M in hexanes) dropwise. The mixture was stirred for 20 min before MeMgI (7.20 mL, 9.10 mmol, 1.26 M in Ether) was added. The reaction mixture was stirred for 15 min before CuCN (0.200 g, 2.20 mmol) was added. To the reaction mixture was added a solution of **9** (0.840 g, 2.20 mmol) in THF (15 mL) slowly. The reaction mixture was kept on stirring for 20 min before MeI (2.7 mL, 44.0 mmol) was added. The reaction mixture was allowed to warm to r.t. in 10 min and Hexanes (100 mL) was added into the violently stirred reaction mixture and then the solution was decanted. The reaction flask was rinsed with Hexanes (2 X 50 mL) and the combined organic solution was washed with brine (40 mL), dried, filtered and concentrated *in vacuo*. The product was purified by column chromatography to afford 1.17 g (78%) of **10** as colorless oil. (**Note:** **10** is readily hydrolyzed on a regular silica gel column. To successfully purify the compound, the silica gel column had to be saturated with NEt₃ by flashing the column with a solvent mixture of 1 : 20 NEt₃ and Hexanes and followed by flashing the column with pure Hexanes to reduce the polarity of the solvent left in the column. **10** was loaded onto the column and the column was flashed with pure Hexanes to remove the tin byproduct and then was flashed with 1:20 NEt₃, Hexanes solvent

mixture to get the purified compound **10**.) R_f 0.38 (EtOAc: hexanes = 1:20); IR 3071, 3049, 2955, 2927, 2856 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ_{H} 7.67 (d, 4 H, J = 6.8 Hz), 7.43-7.35 (m, 6 H), 6.01 (s, 1 H), 5.56 (m, 1 H), 4.61 (d, 1 H, J = 14.2 Hz), 4.51 (d, 1 H, J = 14.2 Hz), 4.08 (m, 1 H), 3.69 (m, 2 H), 2.69 (dd, 1 H, J = 15.9, 6.4 Hz), 2.57 (dd, 1 H, J = 16.6, 6.8 Hz), 1.87 (s, 3 H), 1.53-1.45 (m, 6 H), 1.30 (m, 6H), 1.06 (s, 9 H), 1.93-0.86 (m, 15 H); ^{13}C NMR (100 MHz, CDCl_3) δ_{C} 150.35, 139.16, 135.66, 133.62, 129.74, 129.66, 129.63, 127.68, 125.99, 78.05, 69.77, 66.07, 36.77, 29.24, 27.32, 26.84, 24.65, 19.28, 13.73, 10.21; ^{119}Sn NMR (149 MHz, CDCl_3) δ_{Sn} -56.7;

11

tert-Butyl-[4-(3-iodo-2-methyl-allylidene)-tetrahydro-furan-2-ylmethoxy]-diphenylsilane (11**)**

To a solution of **10** (0.980g, 1.44 mmol) in CH_2Cl_2 (50 mL) was added a solution of I_2 (0.400g, 1.58 mmol) in CH_2Cl_2 (20 mL). The reaction mixture was washed with saturated $\text{Na}_2\text{S}_2\text{O}_3$ solution (20 mL) and saturated NH_4F solution (2 X 20 mL). The organic layer was washed with brine (30 mL), dried, filtered and concentrated *in vacuo*. The product was purified by column chromatography (EtOAc: hexanes = 1:20) to afford 0.710 g (95%) of **11** as colorless oil. R_f 0.29 (EtOAc: hexanes = 1:20); IR 3069, 3049, 2955, 2929, 2857 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ_{H} 7.71-7.66 (m, 4 H), 7.45-7.37 (m, 6 H), 6.02 (s, 1 H), 5.96 (m, 1 H, J = 2.0 Hz), 4.53 (d, 1 H, J = 14.2 Hz), 4.42 (d, 1 H, J = 14.2 Hz), 4.11 (m, 1 H), 3.71 (m, 2 H), 2.67 (dd, 1 H, J = 16.1, 6.0 Hz), 2.55 (dd, 1 H, J = 16.1, 6.0 Hz), 1.94 (s, 3 H), 1.06 (s, 9 H); ^{13}C NMR (100 MHz, CDCl_3) δ_{C} 144.71, 141.47, 135.66, 133.56, 129.74, 127.73, 121.58, 80.68, 78.17, 69.71, 66.00, 36.64, 26.87, 24.08, 19.31;

S-2

[4-(3-Iodo-2-methyl-allylidene)-tetrahydro-furan-2-yl]-methanol (S-2**)**

To a solution of **11** (0.680 g, 1.31 mmol) in THF (20 mL) at 0 °C was added a TBAF solution (1.44 mL, 1.44 mmol, 1 M in THF). The reaction mixture was allowed to warm to r.t. and was stirred for 3 h. Water (30 mL) and EtOAc (50 mL) was then added to the reaction mixture and the two layers were separated. The aqueous layer was washed with EtOAc (2 X 30 mL) and the combined organic layers were washed with brine (30 mL), dried, filtered and concentrated *in vacuo*. The product was purified by column chromatography (EtOAc: hexanes = 1:1) to afford 0.312 g (85%) of **S-2** as a white solid, mp.: 79.0-80.4 °C; R_f 0.20 (EtOAc: hexanes = 1:2); IR 3413, 3046, 2940, 2917, 2869 cm^{-1} ;

^1H NMR (500 MHz, CDCl_3) δ_{H} 5.98 (s, 1 H), 5.92 (s, 1 H), 4.50 (d, 1 H, $J = 14.2$ Hz), 4.35 (d, 1 H, $J = 14.2$ Hz), 4.00 (m, 1 H), 3.65 (dd, 1 H, $J = 11.8, 3.2$ Hz), 3.51 (dd, 1 H, $J = 11.8, 5.8$ Hz), 2.84 (s, 1 H), 2.53 (dd, 1 H, $J = 16.1, 6.4$ Hz), 2.41 (dd, 1 H, $J = 16.0, 8.2$ Hz), 1.88 (s, 3 H); ^{13}C NMR (125 MHz, CDCl_3) δ_{C} 144.42, 140.56, 122.02, 81.08, 78.46, 69.38, 63.76, 35.55, 24.00; HRMS calcd for $\text{C}_9\text{H}_{13}\text{IO}_2$ (M) $^+$ 279.9960, found: 279.9955.

12

4-(3-Iodo-2-methyl-allylidene)-tetrahydro-furan-2-carboxylic acid (12)

To a solution of $(\text{COCl})_2$ (0.47 mL, 0.94 mmol, 2 M solution in CH_2Cl_2) in CH_2Cl_2 (3.5 mL) at -60°C was added a solution of DMSO (0.146) in CH_2Cl_2 (1 mL). The reaction mixture was stirred for 2 min and a solution of **S-2** (0.238 g, 0.85 mmol) in CH_2Cl_2 (2 mL) was added slowly within 5 min. The stirring was continued for an addition 15 min before NEt_3 (0.6 mL, 4.25 mmol) was added. The reaction mixture was stirred for 5 min and then was allowed to warm to r.t. The reaction mixture was concentrated and then was taken by EtOH (1.5 mL). To this mixture at 0°C was slowly added an aqueous solution of AgNO_3 (0.860 g, 5.06 mmol in 3.4 mL water) followed by an aqueous solution of KOH (0.423 g, 7.6 mmol in 1.8 mL water). The reaction mixture was stirred for 15 h and then was filtered through a pad of Celite. The reaction flask and the Celite were rinsed with water (2 X 20 mL). The combined filtrates were acidified at 0°C with 2N HCl aqueous solution till pH got to 2. The aqueous solution was extracted with ether (5 X 30 mL). The combined organic layers were dried, filtered and concentrated *in vacuo* to afford 0.215 g (86%) of **12** as a white solid, mp.: $83.4\text{--}86.2^\circ\text{C}$; R_f 0.30 (MeOH: $\text{CH}_2\text{Cl}_2 = 1:50$); IR 3050, 2961, 2923, 1710cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ_{H} 9.18 (s, 1 H), 6.08 (s, 1 H), 6.00 (s, 1 H), 4.66 (d, 1 H, $J = 14.0$ Hz), 4.60–4.52 (m, 2 H), 3.01 (dd, 1 H, $J = 16.2, 8.4$ Hz), 2.78 (dd, 1 H, $J = 16.2, 4.3$ Hz), 1.93 (s, 3 H); ^{13}C NMR (100 MHz, CDCl_3) δ_{C} 176.94, 144.24, 137.31, 123.09, 82.11, 75.20, 69.90, 37.77, 23.87; HRMS calcd for $\text{C}_9\text{H}_{11}\text{IO}_3$ (M) $^+$ 293.9753, found: 293.9747.

13

Imidazol-1-yl-[4-(3-iodo-2-methyl-allylidene)-tetrahydro-furan-2-yl]-methanone (13)

To a solution of **12** (0.392 g, 1.34 mmol) in THF (5 mL) was added CDI (0.260g, 1.60 mmol). The reaction mixture was stirred for 2 h before water (20 mL) and CH_2Cl_2 (40 mL) was added. The two layers were separated and the aqueous layer was washed with

CH₂Cl₂ (2X 20 mL). The combined organic layers were dried, filtered and concentrated *in vacuo* to afford 0.434 g (95%) of **13** as a white solid; m. p.: 101.0-105.0 °C; R_f 0.28 (MeOH: CH₂Cl₂ = 1:50); IR 3158, 3131, 3057, 2964, 2922, 2850, 2360, 2341, 1731, 1568 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ_H 8.27 (s, 1 H), 7.50 (s, 1 H), 7.02 (s, 1 H), 6.05 (s, 1 H), 6.00 (s, 1 H), 5.00 (m, 1 H), 4.56 (s, 2 H), 3.03 (dd, 1 H, *J* = 16.2, 3.3 Hz), 2.95 (dd, 1 H, *J* = 15.6, 7.4 Hz), 1.88 (s, 3 H); ¹³C NMR (100 MHz, CDCl₃) δ_C 168.09, 144.12, 137.10, 136.72, 130.83, 123.46, 116.45, 82.45, 76.61, 70.10, 36.48, 23.87.

S-3

2-Hydroxy-6-[4-(3-iodo-2-methyl-allylidene)-tetrahydro-furan-2-yl]-3,5-dimethylpyran-4-one (S-3)

To a suspension of NaH (0.100 g, 2.44 mmol, 60 % in mineral oil) in THF (6 mL) was added a solution of **14** (0.352 g, 2.44 mmol) in THF (8 mL) dropwise at 0 °C. After 10 min, the reaction mixture was cooled to -78 °C, and n-BuLi (1.12 mL, 2.44 mmol, 2.19 M in hexanes) was added dropwise. The reaction mixture was stirred for 10 min before warm to -10 °C, at which it is stirred for another 10 min. Then the reaction mixture was cooled back to -78 °C and a solution of **13** (0.420 mg, 1.22 mmol) in THF (6 mL) was added. The reaction mixture was stirred for 2 h before it is warmed to -23 °C and stirred for an additional 2h at this temperature. The reaction was quenched by 1 N HCl aqueous solution (5 mL) and diluted with EtOAc (40 mL). The two layers were separated and the aqueous layer was washed with EtOAc (2 X 30 mL). The combined organic layers were washed with brine (30 mL), dried, filtered and concentrated *in vacuo*. The product was purified by column chromatography (EtOAc: hexanes = 1:4) to afford yellow oil (0.418g), which is used in the next step without fully characterization. A mixture of this material and DBU (0.228 g, 1.5 mmol) in benzene (10 mL) was heated at 90 °C for 3 h. The reaction mixture was cooled to r.t. and acidified with 1 N HCl aqueous solution (2 mL) and diluted with water (10 mL) and EtOAc (15 mL). The two layers were separated and the aqueous layers were washed with EtOAc (2 X mL). The combined organic layers were dried, filtered and concentrated *in vacuo*. The product was purified by column chromatography (pure EtOAc) to afford 0.213 g (45%) of **S-3** as a white solid. m.p.: decomp. at 140 °C; R_f 0.26 (MeOH : CH₂Cl₂ = 1:20); IR 3240 (br), 2929, 2360, 1669, 1569 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ_H 7.67 (s, 1 H), 6.05 (s, 1 H), 5.99 (s, 1 H), 4.96 (t, 1 H, *J* = 7.4 Hz), 4.67 (d, 1 H, *J* = 13.8 Hz), 4.25 (d, 1 H, *J* = 13.8 Hz), 2.95 (dd, 1 H, *J* = 16.0, 7.4 Hz), 2.76 (dd, 1 H, *J* = 16.0, 7.0 Hz), 2.04 (s, 3 H), 1.98 (s, 3 H), 1.93 (s, 3 H); ¹³C NMR (100 MHz, CDCl₃) δ_C 165.36, 164.38, 154.34, 144.42, 139.41, 122.37, 109.64, 100.35, 81.51, 73.35, 69.92, 37.37, 23.97, 9.36, 8.74; HRMS calcd for C₁₅H₁₇IO₄ (M)⁺ 388.0172, found: 388.0167

15

2-[4-(3-Iodo-2-methyl-allylidene)-tetrahydro-furan-2-yl]-6-methoxy-3,5-dimethyl-pyran-4-one (15)

To a solution of **S-3** (0.200 g, 0.52 mmol) in CH₂Cl₂ (5 mL) was added MeOSO₂F (0.588 g, 5.2 mmol) dropwise. After 4 h, the reaction mixture was concentrated and taken by CH₂Cl₂ (20 mL). The organic solution was washed by 1 N NaOH aqueous solution, dried, filtered and concentrated *in vacuo*. The product was purified by column chromatography (1:1 = EtOAc: Hexanes) to afford 0.136 g (65%) of **15** as a yellowish solid; R_f 0.25 (EtOAc: Hexanes = 1:1); IR 2955, 2923, 1665, 1597cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ_H 6.11(s, 1 H), 6.06 (t, 1 H, *J* = 2.0 Hz), 5.11 (t, 1 H, *J* = 7.0 Hz), 4.67 (d, 1 H, *J* = 14.0 Hz), 4.55 (d, 1 H, *J* = 14.0 Hz), 3.89(s, 3 H), 2.92 (dd, 1 H, *J* = 16.0, 7.3 Hz), 2.80 (dd, 1 H, *J* = 16.0, 6.3 Hz), 2.00 (s, 3 H), 1.96 (s, 3 H), 1.83 (s, 3 H); ¹³C NMR (100 MHz, CDCl₃) δ_C 180.57, 162.08, 154.74, 144.16, 139.42, 122.43, 120.09, 100.03, 81.92, 73.38, 70.07, 55.27, 37.77, 23.99, 9.44, 6.92; HRMS calcd for C₁₆H₁₉IO₄ (M)⁺ 402.0328, found: 402.0328

16

4-Iodomethylene-tetrahydro-furan-2-carboxylic acid (16)

Followed the same procedure as in preparation of **12**.

White solid, m.p. 64.0-66.2 °C. R_f 0.37 (MeOH: CH₂Cl₂ = 1:8); IR 3069 (br), 2640, 1731cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ_H 11.04 (s, 1 H), 6.04 (s, 1 H), 4.76-4.73 (m, 1 H), 4.41 (d, 1 H, *J* = 14.5 Hz), 4.29 (d, 1 H, *J* = 14.5 Hz), 2.93 (dd, 1 H, *J* = 16.1, 8.2 Hz), 2.76 (dd, 1 H, *J* = 6.0, 3.5 Hz); ¹³C NMR (125 MHz, CDCl₃) δ_C 176.87, 147.76, 77.84, 75.81, 68.41, 37.81; HRMS calcd for C₆H₇IO₃ (M)⁺ 253.9440, found: 253.9436

17

Imidazol-1-yl-(4-iodomethylene-tetrahydro-furan-2-yl)-methanone (17)

Followed the same procedure as in preparation of **13**.

Yellowish solid, m.p.: 85.0-90.0 °C. R_f 0.19 (MeOH: CH_2Cl_2 = 1:9); IR 3394, 3146, 2969, 2842, 2620, 1988, 1596, 1415 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ_{H} 8.21 (s, 1 H), 7.44 (s, 1 H), 6.95 (s, 1 H), 6.04 (s, 1 H), 5.16 (t, 1 H, J = 6.3 Hz), 4.29 (s, 2 H), 3.0 (d, 1 H, J = 16.1 Hz), 2.87 (dd, 1 H, J = 16.1, 7.6 Hz); ^{13}C NMR (125 MHz, CDCl_3) δ_{C} 167.55, 147.28, 137.02, 130.70, 116.39, 79.27, 75.99, 68.78, 36.42

S-4

2-Hydroxy-6-(4-iodomethylene-tetrahydro-furan-2-yl)-3,5-dimethyl-pyran-4-one (S-4)

Followed the same procedure as in preparation of **S-3**.

Yellowish solid, m.p.: decomp. at 160 °C; R_f 0.20 (EtOAc: hexanes = 1:1); IR 3072 (br), 2930, 1669, 1567 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ_{H} 8.37 (s, 1 H), 6.04 (s, 1 H), 5.13 (t, 1 H, J = 7.4 Hz), 4.46 (d, 1 H, J = 14.2 Hz), 4.25 (d, 1 H, J = 14.2 Hz), 2.94 (dd, 1 H, J = 15.7, 8.2 Hz), 2.79 (dd, 1 H, J = 15.7, 6.5 Hz), 2.04 (s, 3 H), 1.98 (s, 3 H); ^{13}C NMR (125 MHz, CDCl_3) δ_{C} 165.62, 164.82, 153.43, 149.50, 110.33, 100.38, 76.07, 75.75, 67.45, 37.53, 9.42, 8.81; HRMS calcd for $\text{C}_{12}\text{H}_{13}\text{IO}_4$ (M) $^+$ 347.9859, found: 347.9845

18

2-(4-Iodomethylene-tetrahydro-furan-2-yl)-6-methoxy-3,5-dimethyl-pyran-4-one (18)
Followed the same procedure as in preparation of **15**.

White solid, m.p.: 118.0-120.5 °C... R_f 0.11 (EtOAc: hexanes = 1:2); IR 2953, 2924, 1665, 1597 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ_{H} 6.13 (m, 1 H, J = 2.2 Hz), 5.34 (dd, 1 H, J = 7.4, 5.7 Hz), 4.49 (d, 1 H, J = 14.4 Hz), 4.36 (d, 1 H, J = 14.4 Hz), 3.92 (s, 3 H), 2.99-2.91 (m, 1 H), 2.80 (dd, 1 H, J = 16.0, 5.1 Hz), 1.99 (s, 3 H), 1.82 (s, 3 H); ^{13}C NMR (100 MHz, CDCl_3) δ_{C} 180.48, 162.14, 154.61, 149.95, 119.99, 100.07, 76.20, 76.14, 67.55, 55.50, 37.98, 9.48, 6.94; HRMS calcd for $\text{C}_{13}\text{H}_{15}\text{IO}_4$ (M) $^+$ 362.0015, found: 362.0013

S-5

2-Methoxy-3,5-dimethyl-6-[4-(3-trimethylsilylprop-2-ynylidene)-tetrahydrofuran-2-yl]-pyran-4-one (S-5)

Followed the same procedure as in preparation of **S-1**. However **18** is much more reactive and reaction is carried out at r.t.

Yellowish solid, m.p.: 80.0-81.8 °C.. R_f 0.24 (EtOAc: hexanes = 1:2); IR 2956, 2928, 1666, 1600 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ_{H} 5.56 (m, 1 H, J = 2.4 Hz), 5.22 (dd, 1 H, J = 7.6, 5.5 Hz), 4.74 (d, 1 H, J = 15.2 Hz), 4.61-4.56 (m, 1 H), 3.93 (s, 3 H), 3.04-2.96 (m 1 H), 2.86-2.80 (m, 1 H), 2.00 (s, 3 H), 1.83 (s, 3 H), 0.17 (s, 9 H); ^{13}C NMR (100 MHz, CDCl_3) δ_{C} 180.53, 162.15, 154.77, 154.27, 119.88, 101.09, 100.98, 99.98, 99.94, 75.02, 71.77, 55.35, 36.21, 9.45, 6.92, -0.03; HRMS calcd for $\text{C}_{18}\text{H}_{24}\text{O}_4\text{Si}$ (M) $^+$ 332.1444, found: 332.1448

19

2-Methoxy-3,5-dimethyl-6-(4-prop-2-ynylidene-tetrahydrofuran-2-yl)-pyran-4-one (19)

To a solution of **S-5** (0.065 g, 0.2 mmol) in THF (10 mL) at 0 °C was added a TBAF solution (0.24 mL, 0.24 mmol, 1 M in THF). The reaction mixture was allowed to warm to r.t. and was stirred for 10 min. Water (10 mL) and EtOAc (20 mL) was then added to the reaction mixture and the two layers were separated. The aqueous layer was washed with EtOAc (2 X 10 mL) and the combined organic layers were washed with brine (10 mL), dried, filtered and concentrated *in vacuo*. The product was purified by column chromatography (EtOAc: hexanes = 1:1) to afford 0.043 g (83%) of **19** as a white solid, m.p.: 119.2-121.4°C... R_f 0.12 (EtOAc: hexanes = 1:2); IR 3287, 3225, 2955, 2926, 1665, 1594 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ_{H} 5.54 (s, 1 H), 5.24 (t, 1 H, J = 6.5 Hz), 4.75 (d, 1 H, J = 15.2 Hz), 4.61 (d, 1 H, J = 15.2 Hz), 3.93 (s, 3 H), 3.14 (s, 1 H), 3.02 (dd, 1 H, J = 16.2, 7.2 Hz), 2.86-2.83 (m, 1 H), 2.00 (s, 3 H), 1.83 (s, 3 H); ^{13}C NMR (125 MHz, CDCl_3) δ_{C} 180.45, 162.07, 155.01, 154.60, 119.87, 99.96, 99.81, 82.28, 79.56, 74.92, 71.63, 55.29, 36.10, 9.39, 6.85; HRMS calcd for $\text{C}_{15}\text{H}_{16}\text{O}_4$ (M) $^+$ 260.1049, found: 260.1046

Aureothin

Aureothin

A mixture of **15** (10.4 mg, 0.026 mmol), **21** (32.0 mg, 0.08mmol), Pd(PPh₃)₄ (1.5 mg, 0.0013 mmol), CuI (1.0 mg, 0.0052 mmol) and CsF (8.0 mg, 0.052 mmol) in DMF (1 mL) was heated at 45 °C for 2 h before water (10 mL) was added. The mixture was extracted with EtOAc(2 X 10 mL). The combined organic layers were washed with saturated NH₄F aqueous solution (5 mL) and brine (5 mL), dried, filtered and concentrated in *in vacuo*. The product was purified by column chromatography (EtOAc: hexanes = 1:1) to afford 7.7 mg (75%) of **aureothin** as a yellowish solid; R_f 0.17 (EtOAc: hexanes = 1:1); IR 2954, 2920, 2850, 2361, 2341, 1665, 1592, 1339cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ_H 8.19 (d, 2 H, *J* = 8.8 Hz), 7.38 (d, 2 H, *J* = 8.8 Hz), 6.36 (s, 1 H), 6.20 (s, 1 H), 5.13 (t, 1 H, *J* = 7.0 Hz), 4.86 (d, 1 H, *J* = 14.0 Hz), 4.74 (d, 1 H, *J* = 14.0 Hz), 3.94(s, 3 H), 3.05 (dd, 1 H, *J* = 16.0, 6.8 Hz), 2.95 (dd, 1 H, *J* = 16.0, 6.4 Hz), 2.04 (s, 3 H), 2.03 (s, 3 H), 1.84 (s, 3 H); ¹³C NMR (125 MHz, CDCl₃) δ_C 180.52, 162.01, 154.56, 146.10, 144.15, 140.62, 138.52, 129.54, 128.33, 125.93, 123.55, 120.18, 100.03, 73.28, 70.07, 55.20, 38.23, 17.69, 9.40, 6.86; HRMS calcd for C₂₂H₂₃NO₆ (M)⁺ 397.1525, found: 397.1518

N-Acetylaureothamine

N-Acetylaureothamine

Followed the same procedure as in preparation of **aureothin**. 6.6 mg **N-Acetylaureothamine** was prepared in 65% yield from 10.0 mg **15**. White solid. R_f 0.29 (pure EtOAc); IR 3252, 2955, 2924, 2852, 1686, 1663, 1590cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ_H 7.48 (d, 2 H, *J* = 8.4 Hz), 7.24 (s, 1 H), 7.21 (d, 2 H, *J* = 8.4 Hz), 6.38 (s, 1 H), 6.15 (s, 1 H), 5.13 (dd, 1 H, *J* = 7.3, 6.3 Hz), 4.85 (d, 1 H, *J* = 14.0 Hz), 4.73 (d, 1 H, *J* = 14.0 Hz), 3.93(s, 3 H), 3.03 (dd, 1 H, *J* = 16.0, 7.0 Hz), 2.90 (dd, 1 H, *J* = 16.0, 6.1 Hz), 2.18 (s, 3 H), 2.02 (s, 3 H), 2.00 (s, 3 H), 1.84 (s, 3 H); ¹³C NMR (100 MHz, CDCl₃) δ_C 180.68, 168.21, 162.16, 155.14, 137.87, 136.50, 134.45, 133.55, 130.06, 129.73, 126.70, 119.96, 119.53, 99.96, 73.22, 70.18, 55.29, 38.28, 24.68, 17.53, 9.47, 6.94; HRMS calcd for C₂₄H₂₇NO₅ (M)⁺ 409.1889, found: 409.1889

Aureonitrile

Aureonitrile

Followed the same procedure as in preparation of **aureothin**. 8.0 mg **aureonitrile** was prepared in 74% yield from 11.5 mg **15**. White solid; R_f 0.13 (EtOAc: hexanes = 1:1); R_f 0.40 (EtOAc: hexanes = 1:2); IR 2955, 2921, 2853, 2224, 2341, 1665, 1592 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ_{H} 7.61 (d, 2 H, $J = 8.3$ Hz), 7.33 (d, 2 H, $J = 8.3$ Hz), 6.31 (s, 1 H), 6.17 (s, 1 H), 5.13 (t, 1 H, $J = 7.0$ Hz), 4.85 (d, 1 H, $J = 14.2$ Hz), 4.72 (d, 1 H, $J = 14.2$ Hz), 3.93 (s, 3 H), 3.04 (dd, 1 H, $J = 16.0, 6.9$ Hz), 2.80 (dd, 1 H, $J = 16.0, 7.3$ Hz), 2.02 (s, 3 H), 2.01 (s, 3 H), 1.84 (s, 3 H); ^{13}C NMR (125 MHz, CDCl_3) δ_{C} 180.54, 162.02, 154.61, 142.09, 140.19, 137.85, 131.97, 129.49, 128.69, 125.97, 120.14, 118.90, 109.99, 100.00, 73.25, 70.06, 55.19, 38.21, 17.60, 9.41, 6.87; HRMS calcd for $\text{C}_{23}\text{H}_{23}\text{NO}_4 (\text{M})^+$ 377.1627, found: 377.1629

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