Supporting information for

Enantiospecific Formal Total Synthesis of (+)-Dihydrokawain-5-ol

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^1H NMR and ^{13}C NMR Spectra of new compounds.

Experimental Procedures and Characterizations.

Melting points are recorded using Büchi B-540 melting point apparatus in capillary tubes and are uncorrected. IR spectra were recorded on PerkinElmer and JASCO FT-IR 410 spectrophotometer. Solid samples were recorded as KBr discs and liquids as neat/thin films on NaCl plates. ^1H (300 and 400 MHz) and ^{13}C (75 and 100 MHz) NMR spectra were recorded on JNM δ -300 and Bruker AMX 400 spectrometers. The chemical shifts (δ ppm) and coupling constants (Hz) are reported in the standard fashion with reference to the internal tetramethylsilane (for ^1H) or the central line (77.0 ppm) of CDCl_3 (for ^{13}C). High resolution mass spectra were recorded on a Micromass Q-TOF micro-mass spectrometer using electron spray ionization mode. Optical rotations were measured using a JASCO P 1020 digital polarimeter and $[\alpha]_D$ values are given in units of $10^{-1} \text{ deg cm}^2 \text{ g}^{-1}$.

(4R,5R)-N-methoxy-N,2,2-trimethyl-5-((E)-3-phenylacryloyl)-1,3-dioxolane-4-carboxamide (7) : To a solution of **6** (2 g, 5.90 mmol) in dry isopropanol was added Cs_2CO_3 (2.3 g, 7.08 mmol) under argon atmosphere and the reaction mixture was stirred for 5 min at room temperature. Then benzaldehyde (0.75 ml, 7.08 mmol) was added dropwise and the solution was stirred for 45 min at the same temperature. After completion of the reaction, it was cautiously quenched by the addition of 5% aqueous citric acid. The reaction mixture was extracted with diethyl ether and the combined organic layers were washed with brine and dried over anhydrous Na_2SO_4 . Evaporation of solvent and silica gel column chromatography of the residue with petroleum ether: ethyl acetate as eluent afforded the enone **7** (**1.47 g, 78%**).

(4R,5R)-5-cinnamoyl-N-methoxy-N,2,2-trimethyl-1,3-dioxolane-4-carboxamide (7): $[\alpha]_D$: -33.2 (c 0.5, CHCl_3). IR (neat): ν_{max} 2988, 2939, 1676, 1608, 1058, 757 cm^{-1} . ^1H NMR (400 MHz, CDCl_3): δ 7.76 (d, J = 16.1 Hz, 1H), 7.56-7.63 (m, 2H), 7.36-7.31 (m, 3H), 7.13 (d, J = 16.1 Hz, 1H), 5.21 (d, J = 4.6 Hz, 1H), 5.1 (d, J = 4.3 Hz, 1H), 3.72 (s, 3H), 3.24 (s, 3H), 1.55 (s, 3H), 1.45 (s, 3H). ^{13}C NMR (100 MHz, CDCl_3): δ 196.5, 170.1, 145.0, 134.3, 131.0, 129.0 (2 $\times$ C), 128.7 (2 $\times$ C), 121.7, 113.0, 81.9, 74.5, 61.7, 32.5, 26.8, 26.5. HRMS (ESI): m/z for $\text{C}_{17}\text{H}_{21}\text{NO}_5 + \text{Na}$, calcd 342.1317; found: 342.1316.

(4R,5R)-5-((R,E)-1-((tert-butyldimethylsilyl)oxy)-3-phenylallyl)-N-methoxy-N,2,2-trimethyl-1,3-dioxolane-4-carboxamide (10):

To a solution of ketone **7** (1.0 g, 3.1 mmol) in methanol (10 mL), was added $\text{CeCl}_3 \cdot 7\text{H}_2\text{O}$ (1.4 g, 3.7 mmol) and stirred for 15 min at room temperature. NaBH_4 (0.238 g, 6.2 mmol), was then added portion wise over a period of 20 min at -78°C and stirred at the same temperature. After stirring for 1 h, it was quenched by addition of water and extracted with ethyl acetate. The combined organic layers were washed with brine, dried over Na_2SO_4 , concentrated and purified through silica gel column chromatography. Minor diastereomer **8a** was separated, and a mixture of **8** and **9** were proceeded for the next reaction. **0.055g of the minor distereomer was separated by the column chromatography.**

To a pre-cooled (0°C) solution of the alcohols **8** and **9** in CH_2Cl_2 (5 mL) were added DMAP (0.038g, 0.31 mmol), imidazole (0.840 g, 12.0 mmol) followed by TBSCl (0.9 g, 6.2 mmol) under argon atmosphere. The reaction mixture was refluxed for 6 h. After completion of the reaction (TLC), it was poured into cold water (15 mL) and extracted with diethyl ether (2 $\times$ 15 mL). The ethereal layer was washed with brine (10 mL) and dried over anhyd. Na_2SO_4 . Evaporation of the solvent and purification of the resulting crude residue by silica gel column chromatography using petroleum ether/EtOAc (9:1) as eluent furnished **10** (1.3 g, 85%) as a colorless oil. The other side product **11** (0.075 g, 5%) was isolated as its di-TBS ether.

$[\alpha]_D$: -15.0 (c 1.0, CHCl_3). IR (neat): ν_{max} 2955, 1857, 1673, 1254, 776, 695 cm^{-1} . ^1H NMR (400 MHz, CDCl_3):

δ 7.39-7.17 (m, 5H), 6.64 (d, J = 16.0 Hz, 1H), 6.33 (dd, J = 16.0, 5.6 Hz, 1H), 4.76 (brs, 1H), 4.65 (brs, 1H), 4.65-4.52 (m, 1H), 3.70 (s, 3H), 3.16 (s, 3H), 1.47 (s, 3H), 1.46 (s, 3H), 0.91 (s, 9H), 0.10 (s, 3H), 0.08 (s, 3H). **^{13}C NMR (100 MHz, CDCl_3):** δ 170.2, 136.8, 131.4, 128.5 (2 $\times$ C), 128.2, 127.6, 126.5 (2 $\times$ C), 111.5, 80.8, 72.7, 72.3, 61.8, 32.2, 27.1, 26.3, 25.7 (3 $\times$ C), 18.2, -4.6, -4.9. **HRMS (ESI):** m/z for $\text{C}_{23}\text{H}_{37}\text{NO}_5\text{Si}+\text{Na}$, calcd 458.2339; found: 458.2336.

((4*S*,5*R*)-5-((*R*,*E*)-1-((*tert*-butyldimethylsilyl)oxy)-3-phenylallyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methanol (12): To a pre-cooled (0 °C) solution of the Weinreb amide **10** (0.4 g, 0.9 mmol) in MeOH (10 mL) was added NaBH_4 (0.350 g, 9.0 mmol) portion wise and allowed to stir at room temperature for 5 h. After completion of the reaction (monitored by TLC) it was quenched by addition of water (10 mL) and extracted with EtOAc (2 $\times$ 5 mL). The combined organic layers were washed with brine (5 mL) and dried over anhyd. Na_2SO_4 . Evaporation of the solvent gave the crude residue which was purified by silica gel column chromatography using petroleum ether/EtOAc (9:1) as eluent to furnish **12** (0.320 g, 93%) as colorless oil. **$[\alpha]_D$:** -26.0 (c 3.0, CHCl_3). **IR (neat):** 3472, 2932, 2886, 1253, 836, 695 cm^{-1} . **^1H NMR (400 MHz, CDCl_3):** δ 7.45-7.20 (m, 5H), 6.63 (d, J = 16.0 Hz, 1H), 6.31 (dd, J = 16.0, 5.7, 1H), 4.63 (t, J = 4.7 Hz, 1H), 4.09 (dt, J = 8.8, 4.7 Hz, 1H), 3.94 (dd, J = 8.2, 4.7 Hz, 1H), 3.85-3.63 (m, 2H), 2.45 (brs, 1H), 1.43 (s, 3H), 1.38 (s, 3H), 0.95 (s, 9H), 0.14 (s, 3H), 0.12 (s, 3H). **^{13}C NMR (100 MHz, CDCl_3):** δ 136.5, 131.8, 128.6 (2 $\times$ C), 127.7, 127.4, 126.5 (2 $\times$ C), 109.1, 80.8, 77.4, 72.7, 63.1, 27.2, 27.0, 25.8 (3 $\times$ C), 18.3, -4.6, -5.0. **HRMS (ESI):** m/z for $\text{C}_{21}\text{H}_{34}\text{O}_4\text{Si}+\text{Na}$ calcd 401.2124; found 401.2127.

((4*S*,5*R*)-5-((*R*)-1-((*tert*-butyldimethylsilyl)oxy)-3-phenylpropyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methanol (13): To a solution of **12** (0.3 g, 0.8 mmol) in hexane (5 mL) was added 10% palladium on activated charcoal (54 mg) under argon atmosphere. The reaction mixture was stirred for 1 h under hydrogen atmosphere. It was then filtered through a short pad of Celite^R and the Celite^R pad was washed with diethyl ether (10 mL). Evaporation of the solvent followed by silica gel column chromatography of the resulting residue using petroleum:EtOAc (9:1) as eluent afforded **13** (0.3 g, 99%) as a colorless oil. **$[\alpha]_D$:** +7.1 (c 1.0, CHCl_3). **IR (neat):** ν_{max} 3460, 2951, 2859, 1253, 837, 776 cm^{-1} . **^1H NMR (400 MHz, CDCl_3):** δ 7.34-7.13 (m, 5H), 4.04 (dt, J = 8.4, 4.4 Hz, 1H), 3.93 (dt, J = 8.4, 4.4 Hz, 1H), 3.87 (dd, J = 8.4, 4.4 Hz, 1H), 3.82-3.79 (m, 1H), 3.76-3.63 (m, 1H), 2.87-2.72 (m, 1H), 2.69-2.47 (m, 1H), 2.52 (brs, 1H), 2.08-1.92 (m, 1H), 1.74-1.68 (m, 1H), 1.40 (s, 6H), 0.93 (s, 9H), 0.12 (s, 3H), 0.11 (s, 3H). **^{13}C NMR (100 MHz, CDCl_3):** δ 141.9, 128.4, 128.32 (2 $\times$ C), 128.27, 125.9, 108.7, 80.1, 77.3, 71.7, 62.8, 34.6, 32.5, 27.1, 27.0, 25.9 (3 $\times$ C), 18.1, -4.2, -4.7. **HRMS (ESI):** m/z for $\text{C}_{21}\text{H}_{36}\text{O}_4\text{Si}+\text{Na}$ calcd 403.2281; found 403.2278.

(3*R*,4*R*)-4-((*tert*-butyldimethylsilyl)oxy)-6-phenylhex-1-en-3-ol (14): To a solution of **13** (0.25 g, 0.7 mmol) in dry toluene were added triphenylphosphine (0.55 g, 2.1 mmol), imidazole (0.10 g, 1.4 mmol) and iodine (0.360 g, 1.4 mmol) at room temperature and refluxed for 3 h. After the reaction was complete (TLC), it was poured into water (5 mL) and extracted with EtOAc (3 $\times$ 10 mL). The combined organic layers were washed with saturated sodium thiosulfate solution (5 mL), brine (5 mL) and dried over anhyd. Na_2SO_4 . Silica gel column chromatography of the crude residue obtained after evaporation of the solvent, using petroleum ether:ether (95:5) as eluent gave the iodide which was proceeded without characterization. To a solution of the iodide in absolute ethanol (4 mL) was added zinc dust (0.36 g, 5.6 mmol) at room temperature and the reaction mixture was refluxed for 1 h. After completion of the reaction (TLC), it was filtered through a short pad of Celite^R and the Celite^R pad was washed with CH_2Cl_2 (15 mL). Silica gel column chromatography of the residue obtained after evaporation of the solvent, using petroleum ether:EtOAc (4:1) as eluent furnished the alcohol **14** (0.10 g, 84 %) as a colorless oil.

$[\alpha]_D$: +10.0 (c 1.1, CHCl_3). **IR (neat):** ν_{max} 3449, 2954, 2857, 1471, 1254, 836 cm^{-1} . **^1H NMR (400 MHz,**

CDCl₃: δ 7.37-7.21 (m, 2H), 7.27-7.13 (m, 3H), 5.88 (ddd, J = 16.6, 10.5, 5.8 Hz, 1H), 5.35 (d, J = 17.2 Hz, 1H), 5.22 (d, J = 10.5 Hz, 1H), 4.16-4.04 (m, 1H), 3.68 (q, J = 5.1 Hz, 1H), 2.77-2.73 (m, 2H), 2.39 (d, J = 6.2 Hz, 1H), 2.08-1.89 (m, 1H), 0.94 (s, 9H), 0.11 (s, 3H), 0.09 (s, 3H). **¹³C NMR (100 MHz, CDCl₃)**: δ 142.1, 138.3, 128.4 (2 $\times$ C), 128.3 (2 $\times$ C), 125.8, 116.2, 74.8, 74.3, 35.5, 31.4, 25.9 (3 $\times$ C), 18.1, -4.3, -4.5. **HRMS (ESI)**: m/z for C₁₈H₃₀O₂Si+Na, calcd 329.1919; found: 329.1919.

tert-butyl(((3*R*,4*R*)-4-((4-methoxybenzyl)oxy)-1-phenylhex-5-en-3-yl)oxy)dimethylsilane (15): *p*-Methoxybenzyl trichloroacetimidate (0.17 g, 0.6 mmol) and then camphorsulfonic acid (0.014 g, 0.6 mmol) were added to a solution of alcohol **14** (0.10 g, 0.3 mmol) in dichloromethane (5 mL). After 20 h, the reaction mixture was diluted with diethyl ether and then treated with NaHCO₃. After extraction with diethyl ether, organic phases were dried over Na₂SO₄, filtered and concentrated. Crude product was purified on silica gel using petroleum ether:diethyl ether (9:1) to furnish the pure product **15** (0.1 g, 75 %) as yellow oil.

[α]_D: +6.2 (c 0.35, CHCl₃). **IR (neat)**: 2953, 2855, 1599, 1249, 835, 775 cm⁻¹. **¹H NMR (400 MHz, CDCl₃)**: δ 7.32-7.11 (m, 7H), 6.88 (d, J = 8.4 Hz, 2H), 5.81 (ddd, J = 12.0, 9.6, 5.6 Hz, 1H), 5.37-5.23 (m, 2H), 4.57, 4.32 (ABq, J = 11.6 Hz, 2H), 3.82 (s, 3H), 3.84-3.72 (m, 2H), 2.79-2.64 (m, 1H), 2.64-2.59 (m, 1H), 2.00-1.83 (m, 1H), 1.74-1.59 (m, 1H), 0.91 (s, 9H), 0.6 (s, 3H), 0.1 (s, 3H). **¹³C NMR (100 MHz, CDCl₃)**: δ 159.0, 142.7, 135.2, 130.7, 129.7, 129.3 (2 $\times$ C), 128.4 (2 $\times$ C), 128.3 (2 $\times$ C), 125.6, 118.2, 113.6, 82.7, 73.8, 70.1, 55.3, 34.6, 31.9, 25.9 (3C), 18.2, -4.2, -4.7. **HRMS (ESI)**: m/z for C₂₆H₃₈O₃Si+Na calcd 449.2488; found 449.2487.

(3*R*,4*R*)-4-((4-methoxybenzyl)oxy)-1-phenylhex-5-en-3-ol (4): To a stirred solution of the TBS ether **15** (0.10 g, 0.2 mmol) in dry THF (2 mL) was added TBAF (1.0 M solution in THF), (0.5 mL, 0.5 mmol) at 0 °C under nitrogen atmosphere. The reaction mixture was stirred at the same temperature for 6 h. After completion of the reaction (TLC), it was poured into water (5 mL) and extracted with EtOAc (2 $\times$ 10 mL). The combined organic layers were washed with brine (5 mL) and dried over anhyd. Na₂SO₄. The crude residue obtained after evaporation of the solvent was purified by silica gel column chromatography using petroleum ether:EtOAc (9:1) as eluent to afford alcohol **4** (0.07 g, 96 %) as a colorless oil.

[α]_D: -35.1 (c 1.0, CHCl₃). **IR (neat)**: 3419, 2932, 1611, 1513, 1248, 1033, 699 cm⁻¹. **¹H NMR (400 MHz, CDCl₃)**: δ 7.31-7.12 (m, 7H), 6.88 (d, J = 8.6 Hz, 2H), 5.69 (ddd, J = 17.9, 10.3, 8.0 Hz, 1H), 5.35 (d, J = 10.4 Hz, 1H), 5.30 (d, J = 17.4 Hz, 1H), 4.56, 4.27 (ABq, J = 11.2 Hz, 2H), 3.79 (s, 3H), 3.66-3.48 (m, 2H), 2.89-2.75 (m, 1H), 2.74 (brs, 1H), 2.74-2.59 (m, 1H), 1.83-1.61 (m, 2H). **¹³C NMR (100 MHz, CDCl₃)**: δ 159.2, 142.2, 135.2, 130.0, 129.6 (2 $\times$ C), 128.5 (2 $\times$ C), 128.3 (2 $\times$ C), 125.7, 120.2, 113.8 (2 $\times$ C), 84.2, 72.6, 70.0, 55.3, 34.3, 31.7. **HRMS (ESI)**: m/z for C₂₀H₂₄O₃+Na calcd 335.1623; found 335.1623.

(3*R*,4*R*)-4-((4-methoxybenzyl)oxy)-1-phenylhex-5-en-3-yl acrylate (16): To a pre-cooled (0 °C) stirred solution of **4** (0.07 g, 0.2 mmol) in dichloromethane (3 mL), was added Et₃N (0.1 mL, 0.7 mmol) and DMAP (3 mg, 0.02 mmol) and Acryloyl chloride (0.04 mL, 0.5 mmol). Reaction mixture was then allowed to warm up to room temperature and the reaction mixture was stirred at same temperature for 8 h. After completion of the reaction, the reaction mixture was poured into water (4 mL) and extracted with diethyl ether (2 $\times$ 25 mL). The combined organic layers were washed with brine (10 mL) and dried over Na₂SO₄. Evaporation of solvent gave the crude residue which was purified by silica gel column chromatography using petroleum ether:diethyl ether (95:5) to give **16** (0.065 g, 79%) as a colorless oil.

[α]_D: -18.8 (c 0.9, CHCl₃). **IR (neat)**: 2929, 2862, 1724, 1248, 1035, 700 cm⁻¹. **¹H NMR (400 MHz, CDCl₃)**: δ 7.32-7.06 (m, 7H), 6.85 (d, J = 8.5 Hz, 2H), 6.42 (dd, J = 17.3, 0.9 Hz, 1H), 6.15 (dd, J = 17.3, 10.4 Hz, 1H), 5.83 (dd, J = 10.4, 0.9 Hz, 1H), 5.74 (ddd, J = 17.5, 10.5, 7.4 Hz, 1H), 5.38-5.22 (m, 2H), 5.12 (dt, J = 9.0, 4.7

Hz, 1H), 4.57, 4.29 (ABq, $J = 11.8$ Hz, 2H), 3.93-3.80 (m, 1H), 3.78 (s, 3H), 2.64-2.47 (m, 2H), 2.01-1.66 (m, 2H). **^{13}C NMR (100 MHz, CDCl_3):** δ 165.8, 159.1, 141.4, 134.3, 130.8, 130.1, 129.3 (3 $\times$ C), 128.5, 128.3 (4 $\times$ C), 125.8, 119.4, 113.6, 79.8, 74.6, 69.9, 55.1, 31.7, 31.6. **HRMS (ESI):** m/z for $\text{C}_{23}\text{H}_{26}\text{O}_4 + \text{Na}$ calcd 389.1729; found 389.1726.

(5S,6S)-5-((4-methoxybenzyl)oxy)-6-phenethyl-5,6-dihydro-2H-pyran-2-one (3): To a stirred solution of **16** (0.06 g, 0.2 mmol) in toluene (32 mL) was added Grubbs second generation catalyst (0.014 g, 0.02 mmol) at room temperature and refluxed for 4 h. After completion of the reaction (indicated by TLC), toluene was evaporated under vacuum and the reaction mixture was then filtered through a short pad of Celite and the Celite pad was washed with toluene (3 $\times$ 5 mL). Evaporation of solvent followed by silica gel column chromatography of the resulting residue using petroleum ether:EtOAc (3:2) as eluent yielded **3** (0.04 g, 75%) as a colorless oil.

$[\alpha]_D$: -133.5 (c 0.4, CHCl_3). **IR (neat):** 2922, 2857, 1731, 1616, 1250, 1029 cm^{-1} . **^1H NMR (400 MHz, CDCl_3):** δ 7.32-7.13 (m, 7H), 6.94-6.80 (m, 3H), 6.14 (d, $J = 9.8$ Hz, 1H), 4.55, 4.46 (ABq, $J = 11.5$ Hz, 2H), 4.49-4.22 (m, 1H), 3.86 (dd, $J = 4.9, 3.3$ Hz), 3.81 (s, 3H), 2.92-2.80 (m, 1H), 2.79-2.66 (m, 1H), 2.40-2.25 (m, 1H), 2.10-1.93 (m, 1H). **^{13}C NMR (100 MHz, CDCl_3):** δ 163.3, 159.6, 143.0, 140.9, 129.5 (2 $\times$ C), 129.4, 128.53 (2 $\times$ C), 128.52 (2 $\times$ C), 126.1, 123.8, 114.0 (2 $\times$ C), 79.2, 71.0, 67.3, 55.3, 31.4, 31.0. **HRMS (ESI):** m/z for $\text{C}_{21}\text{H}_{22}\text{O}_4 + \text{Na}$ calcd 361.1416; found 361.1412.

¹³C NMR (100 MHz, CDCl₃) spectrum of 7

¹H NMR (400 MHz, CDCl₃) spectrum of 12

¹³C NMR (100 MHz, CDCl₃) spectrum of 12

¹H NMR (400 MHz, CDCl₃) spectrum of **13**

¹³C NMR (100 MHz, CDCl₃) spectrum of **13**

¹H NMR (400 MHz, CDCl₃) spectrum of **14**

¹³C NMR (100 MHz, CDCl₃) spectrum of **14**

^1H NMR (400 MHz, CDCl_3) spectrum of **15**

^{13}C NMR (100 MHz, CDCl_3) spectrum of **15**

¹H NMR (400 MHz, CDCl₃) spectrum of **4**

¹³C NMR (100 MHz, CDCl₃) spectrum of **4**

*¹H NMR (400 MHz, CDCl₃) spectrum of **16***

*¹³C NMR (100 MHz, CDCl₃) spectrum of **16***

¹H NMR (400 MHz, CDCl₃) spectrum of **3**

¹³C NMR (100 MHz, CDCl₃) spectrum of **3**

¹H NMR (400 MHz, CDCl₃) spectrum of **2**

¹³C NMR (100 MHz, CDCl₃) spectrum of **2**