Supporting Information

Concise Synthesis of Anti HIV-1 Active (+)-Inophyllum B and (+)-Calanolide A by Application of (-)-Quinine-Catalyzed Intramolecular Oxo-Michael Addition

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EXPERIMENTAL

General Procedures. All melting points were measured on a micro melting-point hot stage and are uncorrected. IR spectra were recorded in nujol. ^{1}H and ^{13}C NMR spectra were recorded in $CDCl_3$, and tetramethylsilane (0.00 ppm) and the middle resonance of $CDCl_3$ (77.0 ppm) were used as an internal standard, respectively. FABMS and HRFABMS were recorded with *m*-nitrobenzyl alcohol as a matrix.

5,7-Dihydroxy-4-phenylcoumarin. To an ice-cooled and stirred trifluorosufonic acid (14.7 mL, 0.17 M) were mutually and portionwise (five times) added 1,3,5-trihydroxybenzene (10.0 g, 0.079 mM) and ethyl 3-phenyl-3-oxopropionic acid (14.0 mL, 0.082mM), and then the whole was stirred at room temperature (rt) for 17 h. After addition of water (125 mL) the aqueous mixture was triturated with glass rod and separated solid was filtered and washed with warm water (40-50 °C) to give dihydroxycoumarin as pale yellow powder (20 g, quant.), which was used to next step without purification. A part of solid was recrystallized from ethyl acetate to give pale yellow prisms, mp 236-238 °C (lit. mp 246-247 °C).

Lit. L, L, Wood, L. L.; Sopp, J. *J. Org. Chem*. **1962**, *27*, 3703-3705.

5,7-Dimethoxy-4-phenylcoumarin (15). A mixture of 5,7-dihydroxy-4-phenylcoumarin (1.0 g, 3.93 mM), dimethyl sulfate (1.0 mL, 10.6 mM), and K_2CO_3 (1.34 g, 9.66 mM) in acetone (100 mL) was stirred at rt for 20 h. After adition of 10% NH_4OH aq (20 mL) the whole was stirred at rt for 0.5 h and extracted with ethyl acetate (20 mLx3). The organic solution was washed with water (20 mLx3) and brine (20mL), dried over $MgSO_4$, and evaporated. Recrystallization of the residue from EtOH afforded colorless needles (0.77 g, 69%), mp 169-170 °C (lit. mp 164-165 °C).

Lit. Trost, B. M.; Toste, F. D. *J. Am. Chem. Soc*. **1996**, *118*, 6305-6306.

5,7-Dimethoxy-4-phenyl-8-tigloylcoumarin. A solution of tin (IV) chloride (5.0 mL, 42.7 mM) in CH_2Cl_2 (2.5 mL) was slowly added to a solution of **15** (2.78 g, 10.7 mM) and tigloyl chloride (2.78 g, 21.3 mM) in CH_2Cl_2 (15 mL) under -10 °C, and then the whole was stirred at 8 °C for 3 days. After quenched with water (100 mL) the mixture was extracted with $CHCl_3$ (150 mLx3). The organic solution was successively washed with sat $NaHCO_3$ aq (300 mL), water (300 mL), and brine (300 mL), dried over $MgSO_4$, and evaporated . Washing the residue with Et_2O followed by recrystallization from MeOH afforded pale yellow prisms (1.83 g, 47%), mp 171-175 °C. After evaporation of combined washings and mother liquor the residue was purified by column chromatography on SiO_2 (benzene : ethyl acetate=20 : 1) gave an additional coumarin (0.773 g, 20%; total 2.603 g, 67%), mp 178-179 °C. IR 1735, 1655 cm^{-1}; ^1H NMR δ 1.87 (3H, dif. d, *J*=6.8 Hz, 3'-Me), 1.98 (3H, dif. s, 2'-Me), 3.48 (3H, s, OMe), 3.84 (3H, s., OMe), 5.97 (1H, s, 3-H), 6.25 (1H, s, 6-H), 6.50 (1H, dif. q, *J*=6.8 Hz, 3'-H), 7.25-7.26 (2H, m, ArH), 7.37-7.38 (3H, m, ArH); ^{13}C NMR δ 10.6, 15.1, 55.6, 56.1, 91.4, 106.1, 111.0, 113.1, 126.9, 127.4, 127.9, 139.6, 139.7, 143.2, 152. 9, 155.1, 158.7, 159.8, 156.0, 194.0; EIMS *m/z* 364 (M^+, 35%), 309 (100%); Anal. Calcd for $C_{22}H_{20}O_5$: C, 72.51; H, 5.53. Found: C, 72.14; H, 5.52.

7-Hydroxy-5-methoxy-4-phenyl-8-tigloylcoumarin (16). A suspension of the tigloylcoumarin (5. 59 g, 15.3 mM), MgI_2 (4.63 g, 15.3 mM), and K_2CO_3 (2.12 g, 15.3 mM) in dry benzene (500 mL) was refluxed for 4 days under argon. After quenched with 10% HCl aq (500 mL) under ice-cooling the mixture was extracted with ethyl acetate (500 mLx3). The organic solution was washed with water (500 mL) and brine (500 mL), dried over $MgSO_4$, and evaporated. Washing the residue with Et_2O gave pale yellow powder (4.51 g, 84%), a part of which was purified by column chromatography on SiO_2 (benzene : ethyl acetate=20 : 1) to give colorless prisms, mp 190-195 °C (During the mp measurement the crystal forms were changed at 130-134 °C and TLC showed cyclization to **17**). IR 3199, 1734 cm^{-1}; ^1H NMR δ 1.88 (3H, dq, *J*=6.8, 1.2 Hz, 3'-Me), 1.98 (3H,

dq, *J*=1.2, 1.2 Hz, 2'-Me), 3.47 (3H, s, OMe), 5.99 (1H, s, 3-H), 6.21 (1H, dq, *J*=6.8, 1.2 Hz 37H), 6.26 (1H, s, 6-H), 7.23-7.26 (2H, m, ArH), 7.37-7.39 (3H, m, ArH); ^{13}C NMR δ 13.1, 14.3, 55.6, 96.1, 102.6, 104.3, 112.5, 126.9, 127.5, 128.0, 134.7, 139.6, 139.7, 155.6, 156.5, 159.0, 161.8, 166.6, 200.6; EIMS *m/z* 350 (M^+, 47%); HRFABMS *m/z* 351.1214, calcd for $C_{21}H_{19}O_5$ 351.1233.

5,7-Dihydroxy-4-propylcoumarin. To an ice-cooled and stirred trifluorosufonic acid (1.5 mL, 17 mM) were mutually and portionwise (five times) added 1,3,5-trihydroxybenzene (1.00 g, 7.93 mM) and ethyl 3-propyl-3-oxopropionic acid (1.3 mL, 8.12mM), and then the whole was stirred at rt for 12 h. After addition of ice-water (10 mL) the aqueous mixture was triturated with glass rod and separated solid was filtered and washed with hexane to give dihydroxycoumarin as pale yellow powder (1.49 g, 86%), which was used to next step without purification. A part of solid was recrystallized from ethyl acetate to give pale yellow powder, mp 244 °C (lit. mp 236-238 °C).

Lit. Chenera, B.; West, M. L.; Finkelstein, J. A.; Dreyer, G. B. *J. Org. Chem*. **1993**, *58*, 5605-5606

5,7-Dimethoxy-4-propylcoumarin (7). A mixture of dihydroxycoumarin (3.08 g, 14 mM), dimethyl sulfate (3.3 mL, 34.9 mM), and K_2CO_3 (4.85 g, 2.51 mM) in DMF (60 mL) was stirred at rt for 1 h. After adition of 10% NH_4OH aq (200 mL) the whole was stirred at rt for 1 h and extracted with ethyl acetate (200 mLx3). The organic solution was washed with water (200 mLx3) and brine (200 mL), dried over $MgSO_4$, and evaporated. Washings the residue with hexane afforded colorless solid (3.03 g, 87%), mp 119-120 °C; IR 1707 cm^{-1}; ^{1}H NMR δ 1.01 (3H, t, *J*=7.3 Hz, CH_2*Me*), 1.53-1.66 (2H, m, CH_2C*H*$_2$Me), 2.86 (2H, t, *J*=7.6 Hz, CC*H*$_2CH_2$), 3.85 (3H, s, OMe), 3.87 (3H, s, OMe), 5.98 (1H, s, 3-H), 6.31 (1H, d, *J*=2.5 Hz, 8-H), 6.46 (1H, d, *J*=2.5 Hz, 6-H); EIMS *m/z* 248 (M^+, 100%); Anal. Calcd for $C_{14}H_{16}O_4$: C, 67.73; H, 6.50. Found: C, 67.71; H, 6.49.

5,7-Dimethoxy-4-propyl-8-tigloylcoumarin. A solution of tin (IV) chloride (2.0 mL, 17.1 mM) in CH_2Cl_2 (2.5 mL) was slowly added to a solution of **7** (1.01 g, 4.08 mM) and tigloyl chloride (1.19 g, 10.1 mM) in CH_2Cl_2 (5 mL) under -10 °C, and then the whole was stirred under ice-cooling

for 7 days. After quenched with ice-water (10 mL) the mixture was evaporated. to dryness. Washing the residue with EtOH afforded colorless prisms (0.613 g, 46%), mp 145-149 °C. After evaporation of washings the residue was purified by column chromatography (benzene : ethyl acetate=20 : 1) followed by recrystallization from EtOH gave an additional coumarin as colorless prisms (0.377 g, 26%; total 1.00g, 72%). IR 1718, 1654 cm^{-1}; ^1H NMR δ 1.02 (3H, t, *J*=7.3 Hz, CH_2Me), 1.62 (2H, tq, J=7.3, 7.3 Hz, $CH_2C\underline{H}_2Me$), 1.84 (3H, d, *J*=7.1 Hz, 3'-Me), 1.95 (3H, s, 2'-Me), 2.85 (2H, t, J=7.5 Hz, (C)CH_2CH_2), 3.85 (3H, s, OMe), 3.95 (3H, s, OMe), 5.95 (1H, s, 3-H), 6.33 (1H, s, 6-H), 6.43 (1H, qq, *J*=7.1, 1.3 Hz, 3'-H); ^{13}C NMR δ 10.6, 14.1, 15.1, 22.8, 38.6, 56.0, 56.1, 91.1, 103.8, 111.0, 111.2, 139.6, 143.1, 153.1, 157.6, 159.1, 159.2, 160.2, 194.3; Anal. Calcd for $C_{19}H_{22}O_5$: C, 69.07; H, 6.71. Found: C, 68.95; H, 6.80.

7-Hydroxy-5-methoxy-4-propyl-8-tigloylcoumarin (8). A suspension of the tigloylcoumarin (6.47 g, 19.6 mM), MgI_2 (5.56 g, 19.6 mM), and K_2CO_3 (3.70 g, 26.8 mM) in dry benzene (500 mL) was refluxed for 4 days under argon. After quenched with 10% HCl aq (300 mL) under ice-cooling the mixture was extracted with ethyl acetate (300 mLx3). The organic solution was washed with water (300 mL) and brine (300 mL), dried over $MgSO_4$, and evaporated. Washing the residue with Et_2O gave pale yellow powder (5.63 g, 91%), mp 122-124 °C (After measurement of mp TLC showed cyclization to **9**). IR 3199, 1734 cm^{-1}; ^1H NMR δ 1.02 (3H, t, *J*=7.3 Hz, $CH_2\underline{Me}$), 1.62 (2H, dif.tq, *J*=7.3 Hz, $CH_2C\underline{H}_2Me$), 1.84 (3H, dd, *J*=7.0, 1.2 Hz, 3'-Me), 1.98 (3H, d, *J*=1.1 Hz, 2'-Me), 2.86 (2H, t, J=7.5 Hz, (C)C$\underline{H}_2CH_2$), 3.94 (3H, s, OMe), 5.98 (1H, s, 3-H), 6.16 (1H, qq, *J*=7.0, 1.2 Hz 37H), 6.36 (1H, s, 6-H); ^{13}C NMR δ13.0, 14.1, 14.4, 22.8, 38.8, 56.2, 96.1, 103.5, 104.7, 110.7, 134.9, 139.4, 156.3, 158.1, 159.4, 162.3, 165.5, 200.5; EIMS *m/z* 316 (M^+, 47%); HRFABMS *m/z* 317.1361, calcd for $C_{18}H_{21}O_5$ 317.1389.

Conditions for Chiral HPLC

(8*S*,9*S*)-8,9-Dihydro-8,9-dimethyl-5-methoxy-4-phenyl-2*H*,10*H*-benzo[1,2-*b*;5,6-*b'*]dipyran-2,10-dione [*trans*-(-)-17]. DAICEL CHIRALPAK AD-RH (MeOH: 1 mL/min, 254 nm): 9.6 and 13.2 min, 47% ee of the former peak.

(8*R*,9*S*)-8,9-Dihydro-8,9-dimethyl-5-methoxy-4-phenyl-2*H*,10*H*-benzo[1,2-*b*;5,6-*b'*]dipyran-2,10-dione [*cis*-(+)-17]. DAICEL CHIRALPAK AD-RH (MeOH: 0.2 mL/min, 254 nm): 42.9 and 46.2 min, 97% ee of the latter peak.

(10*R*,11*R*)-10,11-Dihydro-4-phenyl-6,6'10,11-tetramethyl-2*H*,6*H*,12*H*-benzo[1,2-*b*;3,4-*b'*;5,6-*b''*]tripyran-2,12-dione [(+)-Inophyllum C] [*trans*-(+)-19] DAICEL CHIRALPAK AD-RH (MeOH: 1 mL/min, 254 nm): 4.6 and 5.9 min, 88% ee of the latter peak.

(10*R*,11*S*)-10,11-Dihydro-4-phenyl-6,6'10,11-tetramethyl-2*H*,6*H*,12*H*-benzo[1,2-*b*;3,4-*b'*;5,6-*b''*]tripyran-2,12-dione [(+)-Inophyllum E] [*cis*-(+)-19]: DAICEL CHIRALPAK AD-RH (MeOH: 0.1 mL/min, 254 nm): 45.9 and 51.9 min, 84% ee of the former peak.

(8*S*,9*S*)-8,9-Dihydro-8,9-dimethyl-5-methoxy-4-propyl-2*H*,10*H*-benzo[1,2-*b*;5,6-*b'*]dipyran-2,10-dione [*trans*-(-)-9]: DAICEL CHIRALPAK AD-RH (MeOH: 0.2 mL/min, 254 nm): 20.3 and 22.3 min, 39% ee of the former peak.

(8*R*,9*S*)-8,9-Dihydro-8,9-dimethyl-5-methoxy-4-propyl-2*H*,10*H*-benzo[1,2-*b*;5,6-*b'*]dipyran-2,10-dione [*cis*-(+)-9]: DAICEL CHIRALPAK AD-RH (MeOH: 0.2 mL/min, 254 nm): 17.9 and 19.3 min, 98% ee of the former peak.

(10*R*,11*R*)-10,11-Dihydro-4-propyl-6,6'10,11-tetramethyl-2*H*,6*H*,12*H*-benzo[1,2-*b*;3,4-*b'*;5,6-*b''*]tripyran-2,12-dione [*trans*-(+)-13]: DAICEL CHIRALPAK AD-RH (MeOH: 0.2 mL/min, 254 nm) 14.0 and 15.1 min, 90% ee of the latter peak.