Supporting Information

Application of a Rhodium-catalyzed Cyclization Cycloaddition Cascade Strategy to the Total Synthesis of (–)-Curcumol

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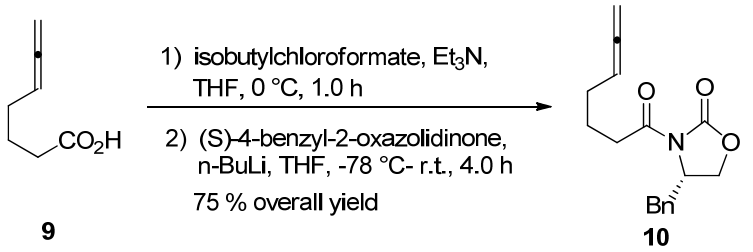
General Experimental.

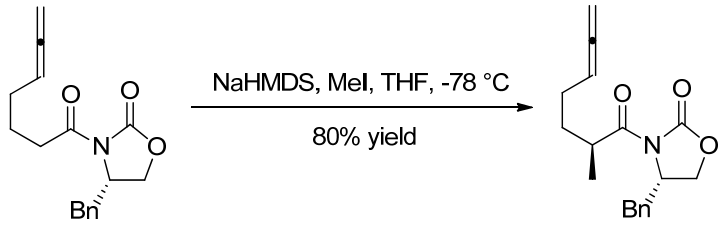
All anhydrous reactions were performed in oven-dried glassware under a positive pressure of dry argon. Air or moisture-sensitive reagents and anhydrous solvents were transferred with oven dried syringes or cannula using standard inert atmosphere techniques. Tetrahydrofuran (THF) and diethyl ether were distilled from Na/K/Ph_2CO ketyl under argon. Dichloromethane and diisopropylamine were distilled from calcium hydride. All chemicals and solvents for reactions were used as received, unless otherwise mentioned. Flash column chromatography was performed on E. Merck silica gel 60 (230-400 mesh ASTM) using EtOAc / *n*-hexane as eluents. Infrared spectra were recorded on a Bio-Rad FT-IR spectrometer from 4000 cm^{-1} to 400 cm^{-1}. All ^1H and ^{13}C NMR spectra were recorded on a Bruker 300 DRX spectrometer, AV400 spectrometer, or 500 DRX spectrometer, operating at 300 MHz, 400 MHz, or 500 MHz respectively for ^1H, and at 75 MHz, 100 MHz, or 125 MHz respectively for ^{13}C. All the spectra were calibrated at 7.26 or 0.00 ppm for ^1H spectra (residual $CHCl_3$ or TMS respectively), and 77.16 or 0.00 ppm for ^{13}C spectra. Spectral features are designated as follows: m = multiplet, q = quartet, t = triplet, d = doublet, s = singlet and br = broad. Mass spectra (MS) were obtained from a Finnigan MAT 95 mass spectrometer for both low resolution and high resolution, with accurate mass reported for the molecular ion (M^+) or the next largest fragment ion thereof. Optical rotations were recorded on a Perkin Elmer 343 Polarimeter. Melting points were measured on an Axiolab ZEISS microscope and were uncorrected.



9 **10**

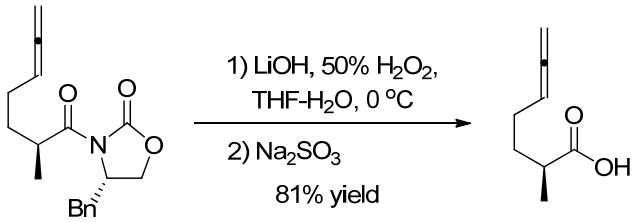
To a solution of acid **9**[1] (5.40 g, 42.8 mmol) in 45 mL of anhydrous THF was added Et_3N (6.0 mL, 43 mmol) at 0 °C, followed by the addition of isobutyl chloroformate (5.85 g, 42.9 mmol) slowly via syringe. The resulting reaction mixture was stirred at 0 °C for 1 h. The reaction mixture was filtered and washed with THF (30 mL). The combined filtrates were cooled in an ice bath, then added dropwise to a solution of (*S*)-4-benzyl-2-oxazolidinone (8.34 g, 47.1 mmol) in 90 mL of anhydrous THF which had been deprotonated by n-BuLi (29.5 mL, 47.1 mmol) at -78 °C under argon. The reaction was allowed to warm to room temperature. After stirring for 4 h, the reaction was quenched by the addition of saturated aq. NH_4Cl. The reaction was extracted with ether. The organics were washed with water, brine, dried over anhydrous $MgSO_4$, and concentrated *in vacuo*. The residue was purified by silica gel flash column chromatography eluting with hexane:EtOAc (v/v 5:1) to afford compound **10** (9.16 g, 75 % yield) as a colourless oil: R_f (35% EtOAc in hexane) 0.71; IR (CH_2Cl_2): 3066, 2931, 1956, 1781, 1702, 1386, 1353, 1211 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.35-7.20 (m, 5H), 5.13 (apparent quintet, *J* = 6.7 Hz, 1H), 4.74-4.64 (m, 3H), 4.22-4.11 (m, 2H), 3.30 (dd, *J* = 13.4, 3.2 Hz, 1H), 2.91-3.06 (m, 2H), 2.77 (dd, *J* = 13.4, 9.6 Hz, 1H), 2.14-2.04 (m, 2H), 1.88-1.81 (m, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 208.7, 173.1, 153.5, 135.3, 129.4, 129.0, 127.3, 89.2, 75.2, 66.2, 55.2, 38.0, 34.8, 27.5, 23.6 ppm; LRMS (EI): *m/z* 285 (M^+, 16), 243 (15), 178 (82), 134 (11); HRMS (EI): Calcd for $C_{17}H_{19}NO_3$ 285.1365; Found 285.1362; $[\alpha]_D^{20}$ = +54.1 (*c* 1.6, $CHCl_3$).

[1] K. K. D. Amarasinghe, and J. Montgomery, *J. Am. Chem. Soc*. 2002**, 124**, 9366; X. Zhang, R. Y. Y. Ko, S. Li, R. Miao, and P. Chiu, *Synlett*, 2006, 1197 – 1200.



10 **11**

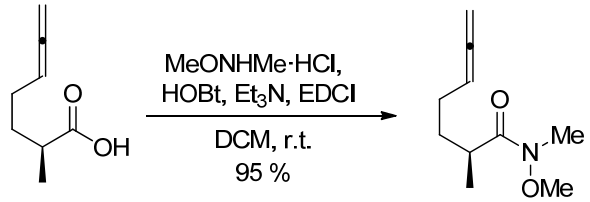
To a solution of compound **10** (5.09 g, 17.8 mmol) in anhydrous THF (150 mL) at -78 °C was added NaHMDS (2.0 M in THF, 11.6 mL, 23.2 mmol). The reaction mixture was stirred at -78 °C for 2 h. CH_3I (2.8 mL, 45 mmol) was added. The resulting reaction mixture was stirred at this temperature overnight. The reaction was allowed to warm to -30 °C, then saturated aq. NH_4Cl was added. The organic layer was separated and the aqueous layer was back-extracted with Et_2O. The combined organics were washed with water, brine, dried over anhydrous $MgSO_4$ and concentrated *in vacuo*. The residue was purified by silica gel flash column chromatography eluting with hexane:EtOAc (v/v 10:1-5:1) to afford compound **11** (4.29 g, 80 % yield) as a colourless oil: R_f (35% EtOAc in hexane) 0.8; IR (CH_2Cl_2): 3065, 3032, 2979, 2935, 2862, 1955, 1779, 1699, 1456, 1386, 1106 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.35-7.20 (m, 5H), 5.08 (apparent quintet, *J* = 6.7 Hz, 1H), 4.70-4.64 (m, 3H), 4.22- 4.14 (m, 2H), 3.81-3.75 (m, 1H), 3.26 (dd, *J* = 13.3, 3.3 Hz, 1H), 2.77 (dd, *J* = 13.4, 9.6 Hz, 1H), 2.06-2.00 (m, 2H), 1.95-1.86 (m, 1H), 1.59-1.52 (m, 1H), 1.24 (d, *J* = 6.9 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 208.6, 177.0, 153.0, 135, 129, 128.9, 127.4, 89.3, 75.1, 66.1, 55.3, 37.9, 32.5, 26.4, 26.0, 17.5 ppm; LRMS (EI): *m/z* 299 (M^+, 12), 208 (17), 190 (7), 178 (64), 166 (32); HRMS (EI): Calcd for $C_{18}H_{21}NO_3$ 299.1521; Found 299.1525; $[\alpha]_D^{20}$ = +64.1 (*c* 1.51, $CHCl_3$).



11 **12**

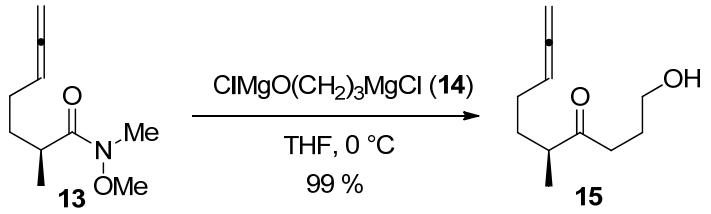
To a solution of **11** (4.293 g, 14.34 mmol) in 50 mL of 4:1 THF-distilled H_2O was added 50% aqueous H_2O_2 slowly at 0 °C, followed by addition of lithium hydroxide monohydrate (1.21 g, 28.7 mmol) in distilled H_2O (20 mL). After the reaction mixture was stirred for 2 h, Na_2SO_3 (10.8 g, 86.0 mmol) in distilled H_2O (30 mL) was added. The bulk of the THF was removed on

a rotatory evaporator and the resulting mixture was extracted with CH_2Cl_2 (3 x 30 mL) to remove the oxazolidinone. The aqueous layer was cooled in an ice bath and acidified to pH 2 by the addition of dilute aqueous HCl. The resulting mixture was extracted with EtOAc (3 x 30 mL). The combined organics were washed with water, brine, dried over anhydrous $MgSO_4$ and concentrated *in vacuo*. The residue was purified by silica gel flash column chromatography eluting with hexane:EtOAc (v/v 3:1) to afford acid **12** (1.635 g, 81 % yield) as a colourless oil: R_f (20% EtOAc in hexane) 0.55; IR (CH_2Cl_2): 3496, 2980, 2940, 1956, 1745, 1707, 1465, 1273,1258 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.09 (apparent quintet, *J* = 6.7 Hz, 1H), 4.72-4.68 (m, 2H), 2.56-2.51 (m, 1H), 2.09-2.03 (m, 2H), 1.59-1.54 (m, 1H), 1.86-1.81 (m, 1H), 1.20 (d, *J* = 7.0Hz, 3H) ppm; ^{13} NMR (100 MHz, $CDCl_3$) δ 208.6, 182.9, 89.2, 75.3, 38.7, 32.6, 25.8, 16.8 ppm; LRMS (EI): *m/z* 140 (M^+, 6), 125 (9), 111 (75), 95 (100); HRMS (EI): Calcd for $C_8H_{12}O_2$ 140.0837; Found 140.0848; $[\alpha]_D^{20}$ = +26.5 (*c* 1.41, $CHCl_3$).

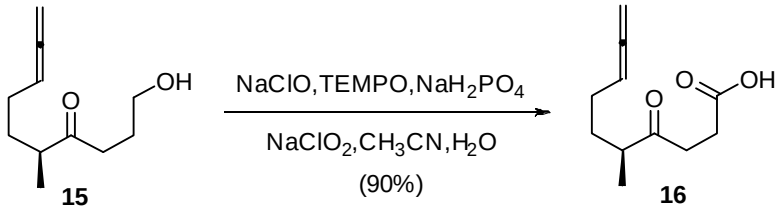


12 **13**

To acid **12** (280.0 mg, 1.997 mmol), MeONHMe·HCl (234 mg, 2.40 mmol) and Et_3N (0.33 mL, 2.4 mmol) in anhydrous CH_2Cl_2 (10 mL) was added HOBt (324 mg, 2.40 mmol). The resulting mixture was stirred until clear. Then EDCI·HCl (460 mg, 2.40 mmol) was added, and the mixture was stirred at room temperature overnight. The reaction mixture was diluted with CH_2Cl_2, then washed with dilute HCl, water, saturated aq. $NaHCO_3$ and dried over anhydrous Na_2SO_4. The organics were concentrated *in vacuo* and the residue was purified by silica gel flash column chromatography eluting with hexane:EtOAc (v/v 10:1) to afford amide **13** (348.0 mg, 95 % yield) as a pale yellow oil: R_f (35% EtOAc in hexane) 0.31; IR (CH_2Cl_2): 2974, 2939, 1955, 1654, 1179, 998, 910 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.09 (apparent quintet, *J* = 6.6 Hz, 1H), 4.63-4.58 (m, 2H), 3.64 (s, 3H), 3.14 (s, 3H), 2.93-2.86 (br m, 1H), 2.06-1.91 (m, 2H), 1.84-1.72 (m, 1H), 1.49-1.38 (m, 1H), 1.07 (d, *J* = 6.9 Hz, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 208.5, 177.6, 89.5, 74.8, 61.3, 34.4, 32.8, 32.2, 26.0, 17.3 ppm; LRMS (EI): *m/z* 152 (M^+-OMe, 8), 132 (67), 108 (11); HRMS (EI): Calcd for $C_9H_{14}NO$ (M^+-OMe): 152.1075; Found 152.1076; $[\alpha]_D^{20}$ = +21.8 (*c* 1.88, $CHCl_3$).

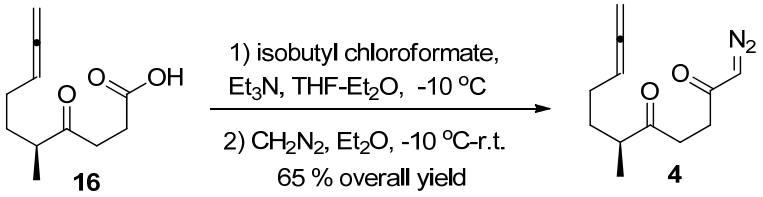


To a solution of amide **13** (336.9 mg, 1.838 mmol) under argon in anhydrous THF (10 mL) was added Grignard reagent $ClMgO(CH_2)_3MgCl$ (**14**) in THF (12.0 mL, ~0.5 M, 6.0 mmol) at 0 °C via cannula. The cooling bath was removed and the resulting solution was stirred at room temperature overnight. The reaction mixture was poured into saturated aq. NH_4Cl. The organic layer was separated and the aqueous layer was extracted with EtOAc. The combined organics were washed with water, brine, dried over anhydrous $MgSO_4$, and concentrated *in vacuo*. The residue was purified by silica gel flash column chromatography eluting with hexane:EtOAc (v/v 3:1-2:1) to afford alcohol **15** (333.0 mg, 99 % yield) as colourless oil: R_f (35% EtOAc in hexane) 0.24; IR (CH_2Cl_2): 3618, 3451, 2979, 2937, 2890, 1956, 1708, 1049, 910 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.01 (apparent quintet, *J* = 6.7 Hz, 1H), 4.69-4.65 (m, 2H), 3.67-3.61 (m, 2H), 2.68-2.51 (m, 3H), 2.02-1.93 (m, 2H),1.87-1.74 (m, 4H), 1.50-1.38 (m, 1H), 1.09 (d, *J* = 7.0 Hz, 3H) ppm ^{13}C NMR (75 MHz, $CDCl_3$) δ 215.1, 208.6, 89.4, 75.2, 62.4, 45.6, 38.1, 32.1, 36.5, 25.9, 16.4 ppm; LRMS (EI): *m/z* 164 (M^+-H_2O, 28), 149 (100), 135 (23), 121 (16), 105(13); HRMS (EI): Calcd for $C_{11}H_{16}O$ (M^+-H_2O) 164.1201; Found 164.1196; $[\alpha]_D^{20}$ = +26.8 (*c* 1.01, $CHCl_3$).



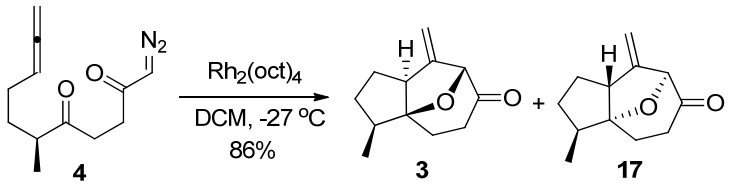
To a solution of alcohol **15** (11.0 g, 60.4 mmol) in 100 mL of acetonitrile and 40 mL of H_2O was added TEMPO (0.66 g, 4.2 mmol), sodium dihydrogen phosphate dihydrate (18.7 g, 120 mmol), sodium chlorite (13.6 g, 120 mmol, 80% purity) and 5% sodium hypochlorite aqueous solution (1.0 mL). The reaction mixture was stirred at room temperature overnight. When the reaction was found to be complete as monitored by TLC analysis, 200 mL of ethyl acetate was added, and the reaction mixture was acidified with 2.0 N HCl to pH 3-4. The organic layer was

separated, and the aqueous layer was back-extracted with 200 mL of ethyl acetate. The combined organics were washed with two 100-mL portions of water, 100 mL of brine, and then concentrated. The residue was purified by silica gel flash column chromatography eluting with hexane:EtOAc (v/v 3:1-2:1) to afford compound **16** (10.6 g, 90 % yield) as a colourless oil: R_f (35% EtOAc in hexane) 0.25; IR (CH_2Cl_2): 3502, 3029, 2983, 2936, 2842, 1956, 1712, 1218 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 9.61 (*br*, 1H), 5.04 (apparent quintet, *J* = 6.7 Hz, 1H), 4.66-4.63 (m, 2H), 2.85-2.72 (m, 2H), 2.65-2.55 (m, 3H), 2.03-1.95 (m, 2H), 1.85-1.75 (m, 1H), 1.47-1.40 (m, 1H), 1.08 (d, *J* = 7.0 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 212.4, 208.5, 178.7, 89.3, 75.2, 45.3, 35.5, 32.0, 27.8, 25.7, 16.2 ppm; LRMS (EI): *m/z* 178 (M^+-H_2O, 2), 135 (10), 123 (11); HRMS (EI): Calcd for $C_{11}H_{14}O_2$ (M^+-H_2O): 178.0994; Found 178.0991; $[\alpha]_D^{20}$ = +25.9 (*c* 0.58, $CHCl_3$).

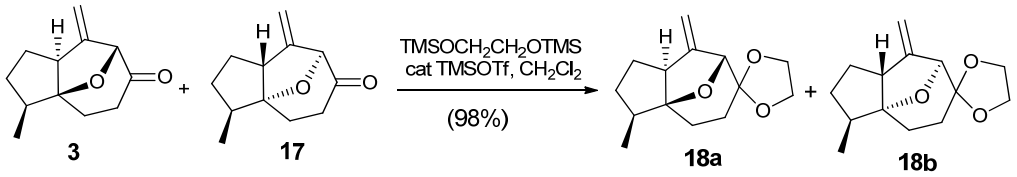


To a mixture of acid **16** (900.1 mg, 4.587 mmol) and Et_3N (0.7 mL, 5.0 mmol) in anhydrous THF (15 mL) and Et_2O (15 mL), was added dropwise isobutyl chloroformate (0.66 mL, 5.0 mmol) at -10 °C. The resulting mixture was stirred at this temperature for 1 h, and freshly prepared CH_2N_2 in Et_2O (30 mL, ~0.5 M, 15 mmol) was added. The cooling bath was removed and the mixture was stirred at room temperature for 4 h. Water was added, and the organic layer was separated. The aqueous layer was back-extracted with Et_2O. The combined organics were washed with water then brine, dried over anhydrous $MgSO_4$ and concentrated *in vacuo*. The residue was purified by silica gel flash column chromatography eluting with hexane:EtOAc (v/v 3:1) to afford diazoketone **4** (656.4 mg, 65 % yield) as a yellow oil: R_f (35% EtOAc in hexane) 0.48; IR (CH_2Cl_2): 3115, 3057, 2975, 2936, 2109, 1956, 1712, 1645, 1378, 1145 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.29 (*br* s, 1H), 5.09 (apparent quintet, *J* = 6.7 Hz, 1H), 4.69-4.65 (m, 2H), 2.91-2.73 (m, 2H), 2.69-2.58 (m, 3H) , 2.03-1.93 (m, 2H), 1.87-1.75 (m, 1H), 1.50-1.39 (m, 1H), 1.09 (d, *J* = 7.0 Hz, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 212.8, 208.6, 193.4, 89.4, 75.2, 54.2, 45.4, 35.5, 33.9, 32.0, 25.8, 16.3 ppm; LRMS (EI): *m/z* 192 (M^+-N_2, 72), 177 (64),

164 (32), 133 (30), 105 (54); HRMS (EI): Calcd for $C_{12}H_{16}O_2$ (M^+-N_2): 192.1150; Found 192.1157; $[\alpha]_D^{20}$ = +35.5 (*c* 0.5, $CHCl_3$).



A solution of diazoketone **4** (656.0 mg, 2.98 mmol) in 10 mL anhydrous CH_2Cl_2 at -27 °C was treated with $Rh_2(oct)_4$ (46.7 mg, 0.0600 mmol). The reaction mixture was stirred for 1 h at this temperature, then allowed to warm to room temperature. The volatiles were removed *in vacuo*. The residue was purified by silica gel flash column chromatography eluting with hexane:EtOAc (v/v 20:1) to afford ketones **3** and **17** (492.4 mg, 86% yield) as an inseparable mixture in the form of a colourless oil.

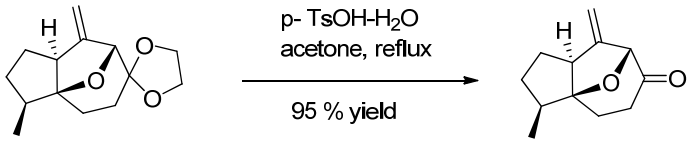


To a mixture of **3** and **17** (399.6 mg, 2.08 mmol) in 15 mL CH_2Cl_2 at –78 °C was added TMSOTf (0.10 mL, 0.55 mmol), and 1,2-bis(trimethylsiloxy)ethane (1.65 g, 7.99 mmol). The reaction mixture was allowed to warm to room temperature. After stirring for 5 h, saturated aq. $NaHCO_3$ was added, and the resulting mixture was extracted with Et_2O. The combined organics were washed with water, brine, dried over anhydrous $MgSO_4$, and concentrated *in vacuo*. The residue was purified by silica gel flash column chromatography eluting with hexane:EtOAc (v/v 10:1-5:1) to afford compound **18a** (159.0 mg, 0.673 mmol) and **18b** (318.6 mg, 1.348 mmol) in 98 % overall yield, both as colourless oils.

18a: R_f (25% EtOAc in hexane) 0.32; IR (CH_2Cl_2): 2958, 1668, 1459, 1253,1045 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.08 (s, 1H), 5.01 (s, 1H), 4.17 (s, 1H), 4.11-3.90 (m, 4H), 2.87 (d, *J* = 10.9 Hz, 1H), 2.18-2.04 (m, 1H), 2.02-1.91 (m, 1H), 1.88-1.78 (m, 1H), 1.76-1.60 (m, 4H), 1.58-1.47 (m, 1H), 1.42-1.34 (m, 1H), 1.05 (d, *J* = 6.0 Hz, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 155.2, 107.4, 106.1, 93.1, 83.6, 65.1, 65.0, 50.0, 42.5, 33.0, 31.9, 30.0, 29.9, 12.4 ppm; LRMS (EI):

m/z 236 (M^+, 96), 174 (11), 137 (100); HRMS (EI): Calcd for $C_{14}H_{20}O_3$ 236.1412; Found 236.1412; $[\alpha]_D^{20}$ = -40.3 (*c* 0.61, $CHCl_3$).

18b: R_f (25% EtOAc in hexane) 0.25; IR (CH_2Cl_2): 2961, 2877, 1668, 1456, 1253,1037 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.05 (s, 1H), 5.01 (s, 1H), 4.18 (s, 1H), 4.08-3.88 (m, 4H), 2.90-2.78 (m, 1H), 2.21-2.03 (m, 3H), 1.99-1.80 (m, 2H), 1.79-1.69 (m, 1H), 1.67-1.57 (m, 1H), 1.51-1.40 (m, 1H), 1.38-1.28 (m, 1H), 0.85 (d, *J* = 7.2 Hz, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 154.3, 107.3, 106.2, 95.2, 83.3, 65.1, 64.8, 49.1, 41.2, 33.7, 31.7, 29.4, 28.5, 15.7 ppm; LRMS (EI): *m/z* 236 (M^+, 90), 174 (14), 137 (100); HRMS (EI): Calcd for $C_{14}H_{20}O_3$ 236.1412; Found 236.1407; $[\alpha]_D^{20}$ = +43.3 (*c* 0.75, $CHCl_3$).

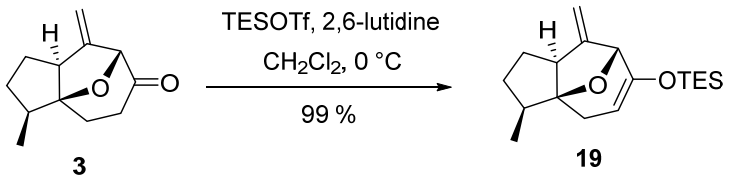


18a **3**

Ketal **18a** (60.2 mg, 0.255 mmol) and *p*-TsOH·H_2O (9.9 mg, 0.052 mmol) in acetone were heated to reflux overnight. The volatiles were removed *in vacuo*. The residue was diluted with Et_2O, washed with saturated aqueous $NaHCO_3$, water, brine, dried over anhydrous $MgSO_4$, and concentrated *in vacuo*. The residue was purified by silica gel flash column chromatography eluting with hexane:EtOAc (v/v 10:1-5:1) to afford ketone **3** (45.6 mg, 95% yield): R_f (10% EtOAc in hexane) 0.63; IR (CH_2Cl_2): 2963, 2869, 1725, 1044, 906 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.18-5.17 (m, 1H), 5.06-5.05 (m, 1H), 4.54 (s, 1H), 3.00 (dt, *J* = 10.9, 1.8 Hz, 1H), 2.51-2.47 (m, 2H), 2.39-2.33 (m, 1H), 2.09-1.84 (m, 1H), 1.83-1.64 (m, 3H), 1.64-1.57 (m, 2H), 1.07 (d, *J* = 6.6 Hz, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ 205.3, 153.6, 108.6, 93.3, 88.0, 50.4, 42.5, 33.6, 32.7, 31.7, 30.9, 11.9 ppm; LRMS (EI): *m/z* 192 (M^+, 100), 164 (63), 149 (53), 135 (19), 121 (21); HRMS (EI): Calcd for $C_{12}H_{16}O_2$ 192.1150; Found 192.1159; $[\alpha]_D^{20}$ = -72.4 (*c* 0.61, $CHCl_3$).

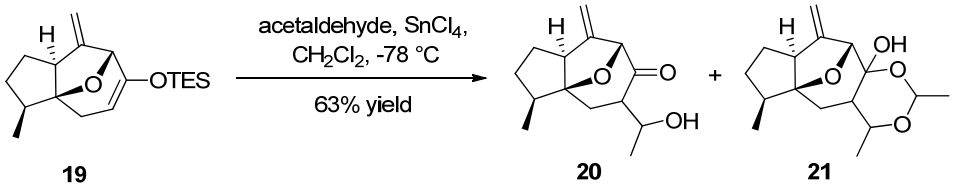
A similar deprotection of **18b** (70.5 mg, 0.298 mmol) afforded **17** (54.8 mg, 95% yield): R_f (10% EtOAc in hexane) 0.60; IR (CH_2Cl_2): 2964, 2878, 1726, 1051, 906 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.16-5.15 (m, 1H), 5.07 (t, *J* = 1.7 Hz, 1H), 4.55 (s, 1H), 2.99-2.97 (m, 1H), 2.51-2.43 (m, 2H), 2.37-2.13 (m, 4H), 1.97-1.92 (m, 1H), 1.60-1.55 (m, 1H), 1.45-1.40 (m, 1H), 0.92 (d, *J* = 7.3 Hz, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ 205.1, 153.1, 108.7, 95.7, 88.0, 49.2, 41.9, 33.3, 32.0, 31.8, 30.1, 15.5 ppm; LRMS (EI): *m/z* 192 (M^+, 100), 164 (28), 149 (91), 135 (37),

121 (11); HRMS (EI): Calcd for $C_{12}H_{16}O_2$ 192.1150; Found 192.1153; $[\alpha]_D^{20}$ = +66.8 (*c* 1.12, $CHCl_3$).



3 **19**

To a solution of **3** (209.4 mg, 1.09 mmol) in CH_2Cl_2 (10 mL) at 0 °C was added 2,6-lutidine (235.7 mg, 2.20 mmol), and TESOTf (436.2 mg, 1.65 mmol) dropwise. After stirring for 1 h at 0 °C, the reaction was quenched by the addition of saturated aq. $NaHCO_3$. The reaction mixture was extracted with Et_2O, and the combined organics were washed with water, brine, dried over anhydrous $MgSO_4$, and concentrated *in vacuo*. The residue was purified by silica gel flash chromatography eluting with hexane:EtOAc (v/v 20:1) to afford enolsilane **19** (330.2 mg, 99% yield) as a colourless oil: R_f (5% EtOAc in hexane) 0.50; IR (CH_2Cl_2): 2959, 2878, 1658, 1459, 1241, 1196, 1050 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 4.91 (d, *J* = 2.5 Hz, 1H), 4.69 (d, *J* = 1.6 Hz, 1H), 4.62 (dd, *J* = 4.8, 2.4, Hz 1H), 4.29 (s, 1H), 2.81 (d, *J* = 10.2 Hz, 1H), 2.66 (dd, *J* = 16.2, 2.4 Hz, 1H), 1.81-1.95 (m, 1H), 1.64-1.75 (m, 4H), 1.53-1.62 (m, 1H), 1.04 (d, *J* = 6.0 Hz, 3H), 0.91-1.03 (m, 9H), 0.62-0.76 (m, 6H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.1, 153.1, 101.9, 97.7, 81.5, 51.5, 42.4, 32.6, 32.1, 31.2, 11.8, 6.8, 5.1 ppm; LRMS (EI): *m/z* 306 (M^+, 69), 277 (100), 236 (38), 209 (48), 115 (36); HRMS (EI): Calcd for $C_{18}H_{30}O_2Si$ 306.2015; Found 306.2012; $[\alpha]_D^{20}$ = -222.7 (*c* 0.77, $CHCl_3$).



19 **20** **21**

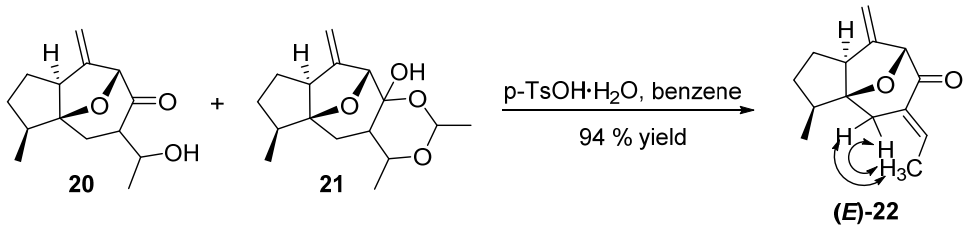
To a solution of acetaldehyde (29.1 mg, 0.661 mmol) in 5.0 mL CH_2Cl_2 at -78 °C was added $SnCl_4$ (143.3 mg, 0.55 mmol) dropwise under argon. The resulting mixture was stirred for 30 min at -78 °C. A solution of **19** (168.3 mg, 0.551 mmol) in CH_2Cl_2 (5.0 mL) was added via cannula under argon. The reaction was stirred for 4 h, then quenched by the addition of saturated aq. $NaHCO_3$. The reaction mixture was extracted with Et_2O. The combined organics were washed with water, brine, dried over anhydrous $MgSO_4$, and concentrated *in*

vacuo. The residue was purified by silica gel flash chromatography eluting with hexane:EtOAc (v/v 20:1-5:1) to afford compound **20** (36.4 mg, 28% yield), and **21** (54.1 mg, 35% yield) as two diastereomers **21a** and **21b**. In addition, compound **3** (33.0 mg) was also recovered from chromatography. Based on recovered **3**, the yields of **20** and **21** were 40% and 51% respectively.

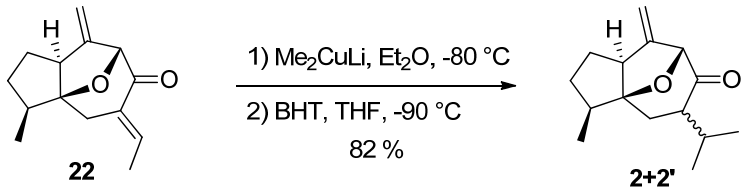
20: colourless oil, R_f (20% EtOAc in hexane) 0.30; IR (CH_2Cl_2): 3524, 2963, 2875, 1710, 1663, 1619, 1459, 1406, 1058 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.17 (dd, *J* = 2.3, 1.1 Hz, 1H), 5.10 (t, *J* = 1.6 Hz, 1H), 4.50 (s, 1H), 4.09-3.98 (m, 2H), 3.06 (d, *J* = 10.9 Hz, 1H), 2.54-2.41 (m, 1H), 2.17-1.91 (m, 2H), 1.88-1.77 (m, 3H), 1.75-1.56 (m, 2H), 1.12 (d, *J* = 7.1 Hz, 3H), 1.04 (d, *J* = 6.4 Hz, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 208.8, 153.0, 109.4, 93.6, 87.7, 68.7, 50.4, 49.7, 42.5, 35.7, 32.8, 31.7, 19.6, 12.1 ppm; LRMS (EI): *m/z* 236 (M^+, 28), 153 (100), 135 (34), 107 (13); HRMS (EI): Calcd for $C_{14}H_{20}O_3$ 236.1412; Found 236.1412; $[\alpha]_D^{20}$ = -70.5 (*c* 3.56, $CHCl_3$).

21a: colourless oil, R_f (20% EtOAc in hexane) 0.52; IR (CH_2Cl_2): 3541, 2963, 2876, 1710, 1459, 1422, 897 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.47 (q, *J* = 5.2 Hz, 1H), 5.13 (d, *J* = 1.0 Hz, 1H), 5.05 (t, *J* = 1.3 Hz, 1H), 4.10 (s, 1H), 4.08-3.96 (m, 1H), 3.47 (s, 1H), 2.86 (dd, *J* = 11.2, 1.7 Hz, 1H), 2.10-1.94 (m, 1H), 1.92-1.61 (m, 4H), 1.60-1.48 (m, 3H), 1.29 (d, *J* = 5.2 Hz, 3H), 1.09 (d, *J* = 6.3 Hz, 3H), 1.02 (d, *J* = 6.0 Hz, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ152.7, 108.6, 94.9, 94.3, 93.4, 85.3, 71.3, 51.2, 43.9, 42.4, 32.8, 31.7, 30.2, 21.0, 18.3, 12.3 ppm; LRMS (EI): *m/z* 280 (M^+, 13), 236 (37), 218 (41), 153 (84), 135 (100); HRMS (EI): Calcd for $C_{16}H_{24}O_4$ 280.1674; Found 280.1667; $[\alpha]_D^{20}$ = -33.7 (*c* 0.94, $CHCl_3$).

21b: colourless oil, R_f (20% EtOAc in hexane) 0.28; IR (CH_2Cl_2): 3595, 3055, 1607, 1422, 896 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.27 (q, *J* = 5.2 Hz, 1H), 5.10 (d, *J* = 1.4 Hz, 1H), 5.06 (t, *J* = 1.4 Hz, 1H), 4.27 (dd, *J* = 6.6, 2.8 Hz, 1H), 4.09 (s, 1H), 2.77 (d, *J* = 10.6 Hz, 1H), 2.47-2.05 (m, 2H), 2.03-1.91 (m, 1H), 1.80-1.67 (m, 3H), 1.65-1.46 (m, 2H), 1.37 (d, *J* = 5.2 Hz, 3H), 1.10 (d, *J* = 6.8 Hz, 3H), 1.08 (d, *J* = 6.5 Hz, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 154.9, 108.3, 93.7, 93.1, 86.2, 69.8, 50.5, 42.8, 38.1, 32.9, 32.0, 27.7, 21.1, 17.2, 12.3 ppm; LRMS (EI): *m/z* 280 (M^+, 16), 236 (33), 218 (28), 153 (100), 135 (62), 107 (23); HRMS (EI): Calcd for $C_{16}H_{24}O_4$ 280.1674; Found 280.1675; $[\alpha]_D^{20}$ = -72.4 (*c* 1.74, $CHCl_3$).

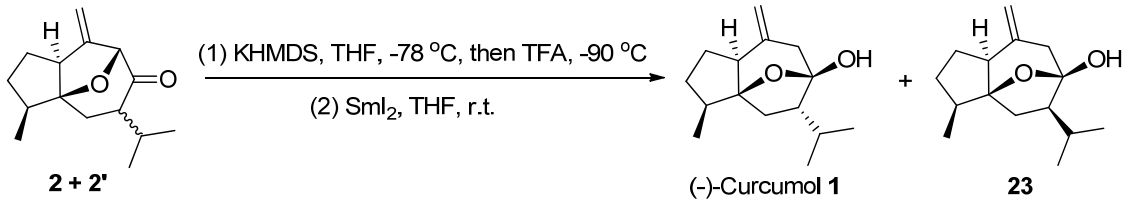


A mixture of **20** (9.9 mg, 0.042 mmol) and **21** (40.1 mg, 0.143 mmol) in benzene was treated with *p*-TsOH·H_2O (6.8 mg, 0.036 mmol) at room temperature. After stirring for 24 h, the reaction was diluted with Et_2O, washed with water, brine, dried over anhydrous $MgSO_4$, then concentrated *in vacuo*. The residue was purified by silica gel flash column chromatography eluting with hexane:EtOAc (v/v 20:1) to afford enone (*E*)-**22** (37.9 mg, 94% yield) as a colourless oil: R_f (20% EtOAc in hexane) 0.52; IR (CH_2Cl_2): 2961, 2934, 2874, 1700, 1620, 1460, 1379, 1052 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.03-6.93 (m, 1H), 5.20 (dd, *J* = 2.6, 1.2 Hz, 1H), 4.98 (dd, *J* = 2.1, 1.3 Hz, 1H), 4.67 (s, 1H), 2.89 (dm, *J* = 16.2 Hz 1H), 2.78 (dm, *J* = 10.5 Hz, 1H), 2.28 (d, *J* = 16.2 Hz, 1H), 2.82-1.91 (m, 1H), 1.89-1.70 (m, 2H), 1.74 (ddd, *J* = 7.3, 1.9, 1.0 Hz, 3H), 1.53-1.67 (m, 2H), 1.10 (d, *J* = 6.4 Hz, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 194.6, 153.5, 139.0, 132.2, 108.3, 92.9, 87.2, 51.3, 42.7, 33.7, 32.5, 31.6, 13.9, 12.0; LRMS (EI): *m/z* 218 (M^+, 100), 203 (18), 189 (84), 175 (22), 161(25), 119 (23) ppm; HRMS (EI): Calcd for $C_{14}H_{18}O_2$ 218.1307; Found 218.1304; $[\alpha]_D^{20}$ = -172.9 (*c* 0.96, $CHCl_3$).



MeLi in Et_2O (0.26 mL, 1.6 M, 0.42 mmol) was added dropwise to a suspension of CuI (38.9 mg, 0.21 mmol) in dry Et_2O (3 mL) at 0 °C, and the resulting solution was stirred at 0 °C for 30 min. This freshly prepared Me_2CuLi in diethyl ether was added dropwise into a solution of enone **22** (14.8 mg, 0.068 mmol) in Et_2O (3.0 mL) at –80 °C. The resulting mixture was stirred for 16 h. The reaction was cooled to –90 °C, and quenched by the addition of a solution of 4-methyl-2,6-di-*tert*-butylphenol (BHT) in THF (2.0 mL). Stirring was continued for 30 min. The resulting mixture was diluted with Et_2O and quenched with saturated aq. NH_4Cl. The organic layer was separated. The aqueous phase was back-extracted with Et_2O. The organic layer was combined and washed with water, brine, dried over anhydrous $MgSO_4$, and concentrated *in*

vacuo. The residue was purified by silica gel flash column chromatography eluting with hexane:EtOAc (v/v 60:1-40:1) to afford **2** + **2'** (13.1 mg, 82% yield, *dr*: 30:70) as a mixture of inseparable diastereomers, in the form of a colourless oil. Data for **2**+**2'**: R_f (2% EtOAc in hexane) 0.35; IR (CH_2Cl_2): 2964, 2871, 1718, 1665, 1467, 1054, 901 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.21 (dd, *J* = 2.6, 1.2 Hz, 0.7H) and 5.15 (dd, *J* = 2.6, 1.2Hz, 0.3H), 5.03 (dd, *J* = 2.6, 1.2Hz, 0.3H) and 4.98 (dd, *J* = 2.1, 1.3 Hz, 0.7H), 4.57 (s, 0.7H) and 4.49(s, 0.3H), 2.65-2.38 (m, 2.7H), 3.02-2.97 (m, 0.3H), 2.82-1.91 (m, 2H), 1.89-1.72 (m, 2H), 1.35-1.12 (m, 1H), 1.10 (d, *J* = 6.4 Hz, 2.0 H) and 1.07 (d, *J* = 6.4 Hz, 1.0 H), 0.92-0.77 (m, 6H) ppm; LRMS (EI): *m/z* 234 (M^+, 30), 191 (18), 173 (42), 137(100); HRMS (EI): Calcd for $C_{15}H_{22}O_2$ 234.1620; Found 234.1622.



2 + 2' (-)-Curcumol **1** **23**

To a mixture of ketone **2**+**2'** (9.2 mg, 0.039 mmol, dr= 30:70) in THF (2.0 mL) at −78 °C was added KHMDS (0.08 mL, 0.08 mmol, 1.0 M in THF) under argon. After stirring for 1 h, the reaction was cooled to –90 °C , and a solution of trifluoroacetic acid (TFA, 11.4 mg, 0.1 mmoL) in THF (1.0 mL) was added dropwise. Stirring was continued at –90 °C for 30 min. The reaction was allowed to warm to room temperature. The resulting mixture was diluted with Et_2O, washed with saturated aqueous $NaHCO_3$, water, brine, dried over anhydrous $MgSO_4$, and concentrated *in vacuo*. The residue was purified by silica gel flash column chromatography eluting with hexane:EtOAc (v/v 60:1-40:1) to afford **2 + 2'** (8.3 mg).

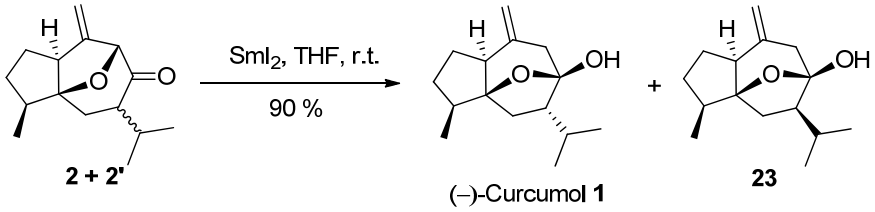
SmI_2 (1.6 mL, 0.16 mmol, 0.1 M in THF) was added into the above mixture of ketones **2+2'** (8.3 mg, 0.036 mmol) at room temperature under argon. The reaction mixture was stirred overnight, then diluted with Et_2O. The reaction mixture was washed with saturated aqueous $NaHCO_3$, water, brine, dried over anhydrous $MgSO_4$, and concentrated *in vacuo*. The residue was purified by silica gel flash column chromatography eluting with hexane:EtOAc (v/v 20:1-10:1) to afford (–)-curcumol **1** (3.7 mg) and **23** (3.8 mg) in 81% yield over two steps.

(–)-curcumol **1**: R_f (10% EtOAc in hexane) 0.35; colourless crystalline needles, mp= 141-142 °C, *Ref*[2] mp= 140-141 °C; IR (CH_2Cl_2): 3577, 2960, 2873, 1646, 1609, 1463, 13.25, 1124 cm^{-1};

[2] L. Zhou, W. Xu, Y. Chen, J. Zhao, N. Yu, B. Fu, and S. You, *Catal. Commun.* 2012, **28**, 191–195.

^{1}H NMR (500 MHz, $CDCl_3$) δ 4.87 (apparent s, 2H), 2.57 (d, *J* = 14.6 Hz, 1H), 2.51 (d, *J* = 14.6 Hz, 1H), 2.17 (dd, *J* = 11.4, 9.0 Hz, 1H), 2.13 (t, *J* = 12.5 Hz, 1H), 1.97-1.91 (m, 1H), 1.90-1.84 (m, 1H), 1.80-1.69 (m, 2H), 1.68-1.61 (m, 1H), 1.52-1.47 (m, 1H), 1.46-1.42 (m, 1H), 1.17 (dd, *J* = 12.5, 6.8 Hz, 1H), 1.00 (d, *J* = 6.5 Hz, 3H), 0.99 (d, *J* = 6.5 Hz, 3H), 0.86 (d, *J* = 6.5 Hz, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ 144.7, 112.9, 104.5, 88.1, 56.5, 54.5, 39.4, 38.8, 34.7, 30.9, 28.7, 28.3, 23.1, 21.5, 12.4 ppm; LRMS (EI): *m/z* 236 (M^+, 31), 193 (49), 165 (13), 147(24), 136 (30), 121 (100) ppm; HRMS (EI): Calcd for $C_{15}H_{24}O_2$ 236.1776; Found 236.1777; $[\alpha]_D^{20}$ = -12.5 (*c* = 0.20, $CHCl_3$), *Ref.*[3] $[\alpha]^{30}_D$= –32.26 (c = 2.13, $CHCl_3$).

23: R_f (10% EtOAc in hexane) 0.40; colourless crystalline needles, mp= 63-64 °C; IR (CH_2Cl_2): 3577, 2960, 2875, 1651, 1470, 1094 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.88 (t, *J* = 2.2 Hz, 1H), 4.83 (t, *J* = 2.2 Hz, 1H), 2.68, (s, 1H, OH), 2.52 (d, *J* = 13.6 Hz, 1H), 2.30 (d, *J* = 13.6 Hz, 1H), 2.21 (dd, *J* = 11.2, 9.1 Hz, 1H), 1.98-1.91 (m, 3H), 1.90-1.84 (m, 1H), 1.75-1.68 (m, 2H), 1.67-1.63 (m, 1H), 1.54-1.48 (m, 1H), 1.44 (dd, *J* = 12.4, 9.1 Hz, 1H), 0.98 (d, *J* = 6.5 Hz, 3H), 0.92 (d, *J* = 6.5 Hz, 3H), 0.90 (d, *J* = 6.5 Hz, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ 145.2, 112.8, 104.4, 88.0, 53.0, 48.0, 45.3, 39.3, 31.8, 31.2, 28.0, 27.5, 22.3, 18.7, 12.5 ppm; LRMS (EI): *m/z* 236 (M^+, 17), 193 (100), 175 (13), 147(32), 135 (25), 121 (71); HRMS (EI): Calcd for $C_{15}H_{24}O_2$ 236.1776; Found 236.1777; $[\alpha]_D^{20}$ = +25.6 (*c* 0.39, $CHCl_3$).



SmI_2 (1.0 mL, ~0.1 M in THF, 0.1 mmol) was added to ketones **2 + 2'** (5.2 mg, 0.022 mmol) under argon at room temperature. The reaction was stirred overnight. The reaction mixture was diluted with Et_2O and washed with saturated aqueous $NaHCO_3$, water, brine, dried over anhydrous $MgSO_4$ and concentrated *in vacuo*. The residue was purified by silica gel flash column chromatography eluting with hexane:EtOAc (v/v 20:1-10:1) to afford **1** (1.2 mg) and **23** (2.8 mg) in 90% overall yield.

[3] K. Harimaya, J. F. Gao, T. Ohkura, T. Kawamata, Y. Iitaka, Y. T. Guo, and S. Inayama, *Chem. Pharm. Bull.*, 1991, **39**, 843-853.