A rhodium carbene cyclization-cycloaddition strategy toward the pseudolaric acids

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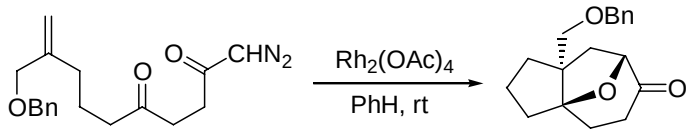
Supporting Information.

Experimental Procedures.

General Experimental. All anhydrous reactions were performed in flame-dried or 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 cannulae using standard inert atmosphere techniques. Flash chromatography was performed with E. Merck silica gel 60 (230-400 mesh ASTM). All chemicals and solvents for reactions were used as received unless otherwise mentioned. Tetrahydrofuran (THF), diethyl ether were distilled from sodium/ benzophenone ketyl under argon. Dichloromethane, benzene, triethylamine, and diisopropylethylamine (DIPEA) were distilled from calcium hydride. Methanol was distilled from magnesium methoxide. Acetone was distilled from potassium carbonate. Dimethylformamide (DMF) and dimethylacetamide (DMA) was distilled from barium oxide under reduced pressure.

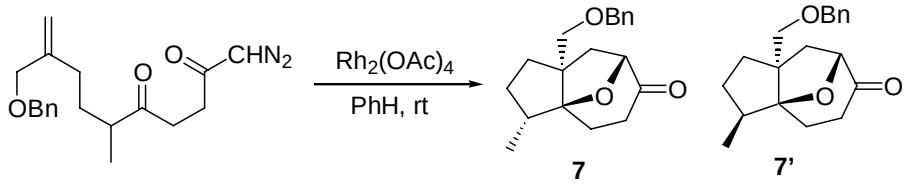
Proton (^{1}H) and carbon-13 (^{13}C) nuclear magnetic resonance spectra were obtained in deuterochloroform ($CDCl_3$) unless otherwise indicated, with tetramethylsilane (TMS) as the internal standard at ambient temperature on a Bruker Avance DPX300 spectrometer operating at 300 MHz for ^{1}H and 75 MHz for ^{13}C, or a Bruker Avance DRX500 spectrometer operating at 500 MHz for ^{1}H and at 125 MHz for ^{13}C. All the spectra were calibrated at δ 0.00 ppm or δ 7.26 ppm for ^{1}H spectra (TMS or residual $CHCl_3$), and δ 0.00 ppm or δ 77.02 ppm for ^{13}C spectra. Splitting patterns are designated as follows: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet and br, broad. Infrared absorption spectra (IR) were recorded on a Bio-Rad FTS 165 spectrometer as a neat film between KBr plates or as a solution in dichloromethane from 4000 cm^{-1} to 400 cm^{-1}. 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 suitable fragment ions. Optical rotations were recorded on a Perkin Elmer 343 Polarimer.



6

A solution of 9-benzyloxymethyl-1-diazo-dec-9-ene-2,5-dione (72 mg, 0.229 mmol) in dry benzene (5 mL) was treated with rhodium (II) acetate (1 mg, 0.00226 mmol) for 6 h at room temperature. The reaction mixture was filtered and concentrated *in vacuo*. The crude oil was purified by flash chromatography on silica gel to give product **6** (40 mg, 61 % yield) as a colorless oil. **6:** R_f = 0.72 (33% EtOAc in hexane); ^{1}H NMR

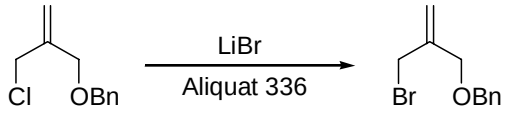
(300 MHz, $CDCl_3$) δ 7.38-7.27 (m, 5H), 4.49 (s, 2H), 4.31 (dd, *J* = 6.0, 3.5 Hz, 1H), 3.32 (d, *J* = 9.2 Hz, 1H), 3.28 (d, *J* = 9.2 Hz, 1H), 2.42 (m, 2H), 2.19 (ddd, *J* = 17.8, 10.1, 6.6 Hz, 1H), 1.97-1.77 (m, 4H), 1.66 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 212.1, 137.9, 128.4, 127.7, 127.6, 92.9, 82.2, 74.0, 73.5, 53.9, 42.4, 39.1, 37.5, 33.7, 26.1, 22.6; IR (film, cm^{-1}): 2955, 2867, 1725, 1444, 1420, 1236 1085, 1042; LRMS (EI): *m/z* 286 (M^+, 8), 195 (17), 150 (25), 137 (13), 123 (10), 119 (12), 95 (19), 91 (100), 79 (12); HRMS (EI): Calculated for $C_{18}H_{22}O_3$: 286.1569; Found: 286.1565.



A solution of 9-benzyloxymethyl-1-diazo-6-methyl-dec-9-ene-2,5-dione (28.7 mg, 0.0874 mmol) in dry CH_2Cl_2 (1.0 mL) was treated with rhodium (II) acetate (0.5 mg, 0.0011 mmol) for 2 h at 0°C. The reaction mixture was filtered and concentrated *in vacuo*. The crude oil was purified by flash chromatography with 5% EtOAc in hexane on silica gel to give diastereoisomer **7** (13.1 mg, 50 % yield) as a colorless oil, and diastereoisomer **7'** (3.4 mg, 13 % yield) as a colorless oil. **7:** R_f = 0.48 (20% EtOAc/hexane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37-7.27 (m, 5H), 4.49 (d, *J* = 12.1 Hz, 1H), 4.46 (d, *J* = 12.1 Hz, 1H), 4.27 (dd, *J* = 8.1, 0.5 Hz, 1H), 3.32 (d, *J* = 9.4 Hz, 1H), 3.29 (d, *J* = 9.4 Hz, 1H), 2.46 (ddd, *J* = 18.0, 11.3, 4.5 Hz, 1H), 2.36 (ddd, *J* = 18.1, 9.1, 4.5 Hz, 1H), 2.17 (m, 3H), 2.01 (dd, *J* = 12.9, 8.2 Hz, 1H), 1.89 (m, 2H), 1.59 (ddd, *J* = 13.1, 7.6, 2.4 Hz, 1H), 1.38 (m, 1H), 0.90 (d, *J* = 7.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 213.2, 137.8, 128.4, 127.76, 127.74, 94.5, 82.1, 74.5, 73.6, 54.4, 43.5, 42.9, 36.7, 33.9, 30.3, 23.8, 14.3; IR (film, cm^{-1}): 2956, 2919, 2871, 1721, 1462, 1105; LRMS (EI): *m/z* 300 (M^+, 33), 257 (10), 209 (18), 191 (24), 164 (66), 151 (83), 147 (100), 133 (42); HRMS (EI): Calculated for $C_{19}H_{24}O_3$ (M^+): 300.1725; Found: 300.1726. The relative stereochemistry of **7** was assigned by its 2-D noe spectrum, in which the methyl group (δ 0.90 ppm) and the benzyloxymethylene protons (δ 3.32, 3.29 ppm) clearly showed the presence of a cross-peak. Therefore the methyl and methylene groups must on the same side of the cyclopentane ring, and the stereochemistry of **7** must be as shown.

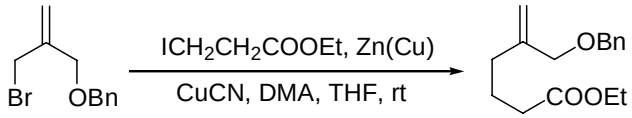
7': R_f= 0.55 (20% EtOAc in hexane); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.37-7.27 (m, 5H), 4.47 (s, 2H), 4.29 (d, *J* = 8.2 Hz, 1H), 3.30 (d, *J* = 9.4 Hz, 1H), 3.25 (d, *J* = 9.4 Hz, 1H), 2.48 (ddd, *J* = 18.0, 11.3, 4.6 Hz, 1H), 2.37 (ddd, *J* = 18.0, 9.2, 4.9 Hz, 1H), 2.19 (ddd, *J* = 13.8, 11.3, 4.9 Hz, 1H), 2.10 (dd, *J* = 13.0, 1.0 Hz, 1H), 1.99 (dd, *J* = 13.0, 8.3 Hz, 1H), 1.71 (m, 3H), 1.59 (m, 3H), 1.05 (d, *J* = 6.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 212.9, 137.9, 128.4, 127.72, 127.65, 93.0, 82.0, 74.4, 73.5, 54.7, 43.2, 41.9, 36.8, 33.9, 30.7, 23.2, 12.6; IR (film, cm^{-1}): 2959, 2870, 1723, 1456, 1364, 1113; LRMS (EI): *m/z* 300 (M^+, 52), 209 (92), 192 (30), 164 (81), 151 (100), 147 (62), 133 (46); HRMS (EI): Calculated for $C_{19}H_{24}O_3$ (M^+): 300.1725; Found: 300.1728. The relative stereochemistry of **7'** was assigned by its 2-D noe spectrum, in which the methyl group (δ 1.05 ppm) and the benzyloxymethylene protons (δ 3.30, 3.25 ppm) clearly showed the absence of a cross-peak, therefore placing these two groups on opposite sides of the cyclopentane ring. The methine

proton was not well resolved and was part of a multiplet at δ 1.59, therefore the presence of a cross-peak between the methine proton and the benzyloxymethylene protons could not be clearly established.



8

To a mixture containing neat (2-chloromethyl-allyloxymethyl)-benzene[1] (7.20 g, 36.64 mmol) and Aliquat 336 (0.70 g, 1.73 mmol) was added anhydrous LiBr (6.38 g, 73.47 mmol). The mixture was heated to 60 ºC and was maintained at 60 ºC for 2h. After cooling, the mixture was filtered on Florisil and washed with Et_2O (3 x 30 mL). The organic solvent was removed to give compound **8** (8.53 g, 97 % yield) as a pale yellow oil, which was used in the next reaction without further purification. **8:** R_f = 0.75 (15% Et_2O in hexane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.38-7.28 (m, 5H), 5.37 (s, 1H), 5.29 (s, 1H), 4.55 (s, 2H), 4.17 (s, 2H), 4.07 (s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 142.4, 138.0, 128.5, 127.7 (2C), 117.3 72.4, 70.3, 33.1; IR (film, cm^{-1}): 2935, 2858, 1612, 1513, 1468, 1252, 1174, 1093, 921, 819; LRMS (EI): *m/z* 161 (M^+ – Br, 23), 91 (100), 81 (56), 79 (61); HRMS (EI): Calculated for $C_{11}H_{13}O$ (M^+ – Br): 161.0966; Found: 161.0965.



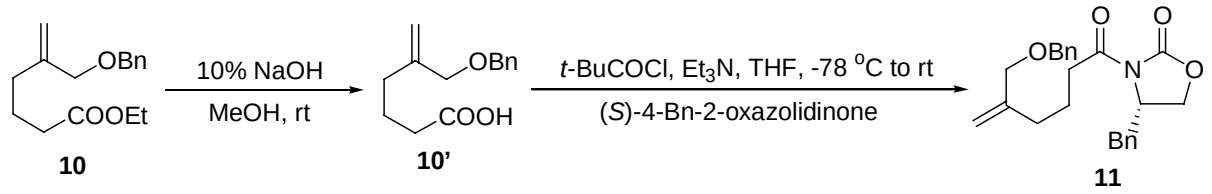
8 **10**

Zinc-copper couple was prepared as described in the literature.[2] 3-Iodo-propionic acid ethyl ester (ICH_2CH_2COOEt) was prepared from the corresponding bromide ($BrCH_2CH_2COOEt$) by a Finkelstein reaction.[3]

A mixture of 3-iodo-propionic acid ethyl ester (9.65 g, 43.86 mmol), Zn(Cu) (3.41 g, 52.46 mmol), *N*, *N*-dimethylacetamide (DMA) (5.64 mL, 62.04 mmol) in THF (50 mL) was stirred at rt for 2 h, then at 60 ºC for 1 h under argon to prepare the zinc ester homoenolate **9**. This reaction mixture was filtered and transferred by cannula to a mixture of compound **8** (8.24 g, 34.19 mmol) and CuCN (0.51 g, 5.70 mmol) in THF (30 mL). After stirring overnight at rt, the mixture was quenched with saturated NH_4Cl. The organic phase was separated, and washed sequentially with saturated $NaHCO_3$, brine, dried over $MgSO_4$ and concentrated *in vacuo*. The residue was purified by flash chromatography on silica gel to give compound **10** (7.84 g, 88 % yield) as a colorless oil. **10:** R_f = 0.35 (15% Et_2O in hexane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.35-7.27 (m, 5H), 5.08 (s, 1H), 4.95 (s, 1H), 4.49 (s, 2H), 4.12 (q, *J* = 7.1 Hz, 2H), 3.96 (s, 2H), 2.31 (t, *J* = 7.5 Hz, 2H), 2.13 (t, *J* = 7.7 Hz, 2H), 1.80 (m, 2H), 1.25 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.6, 145.1, 138.3, 128.4, 127.7, 127.6, 112.4, 73.0, 72.0, 60.3, 33.9, 32.4, 22.8, 14.3; IR (film, cm^{-1}): 2930,

[1] van der Louw, J.; van der Baan, L. L.; de Kanter, F. J. J.; Bickelhaupt, F.; Klumpp, G. W. *Tetrahedron* **1992**, *48*, 6087.
[2] Smith, R. D.; Simmons, H. E. *Org. Synth. Coll. Vol 5*, **1973**, 855.
[3] Sondheimer, F.; Rosenkranz, G.; Mancera, O.; Djerassi, C. *J. Am. Chem. Soc.* **1953**, *75*, 2601.

2856, 1732, 1454, 1373, 1097, 1074, 1029; LRMS (EI): *m/z* 262 (M^+, 5), 231 (11), 171 (19), 156 (41), 91 (100); HRMS (EI): Calculated for $C_{16}H_{24}O_4$: 262.1569; Found: 262.1567.



10 **10'** **11**

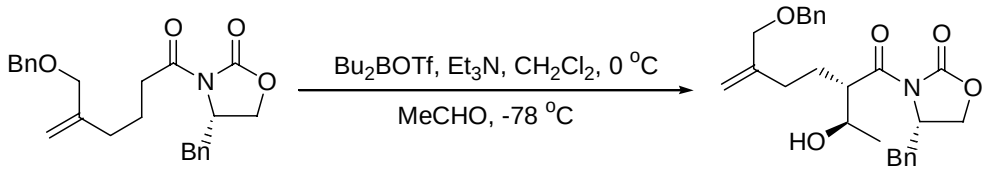
To a solution of ester **10** (7.80 g, 29.77 mmol) in MeOH (60 mL) was added 10% NaOH (30 mL) at room temperature. The resulting mixture was stirred vigorously for 4 h and then methanol was removed on the rotary evaporator. The residue was acidified with 10 % HCl to pH 3 and extracted with EtOAc (3 x 50 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated *in vacuo* to give crude acid **10'** (6.76 g, 97 %) as colorless oil, which was used without further purification. **10':** R_f = 0.15 (40% EtOAc in hexane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.35-7.27 (m, 5H), 5.10 (s, 1H), 4.96 (s, 1H), 4.49 (s, 2H), 3.96 (s, 2H), 2.38 (t, *J* = 7.4 Hz, 2H), 2.15 (t, *J* = 7.5 Hz, 2H), 1.82 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 179.4, 144.8, 138.2, 128.4, 127.7, 127.6, 112.6, 72.9, 72.0, 33.4, 32.3, 22.5; IR (film, cm^{-1}): 3444 (br), 2940, 2867, 1709, 1454, 1274, 1096, 1072, 910. LRMS (EI): *m/z* 234 (M^+, 2), 143 (9), 128 (25), 125 (18), 107 (60), 91 (100); HRMS (EI): Calculated for $C_{14}H_{18}O_3$: 234.1256; Found: 234.1259.

(*S*)-4-benzyl-2-oxazolidinone was prepared as described in literature.[4]

To a flask containing acid **10'** (10.38 g, 44.36 mmol) and triethylamine (6.78 mL, 48.87 mmol) in THF (100 mL) at –78 ºC was added slowly pivaloyl chloride (6.08 mL, 48.87 mmol) under argon. The thick white paste was allowed to stir at 0 ºC for 1 h. In a separate flask, (*S*)-4-benzyl-2-oxazolidinone (7.80 g, 44.07 mmol) was dissolved in THF (100 mL) at room temperature. DMAP (0.70 g, 5.738 mmol) was added, followed by triethylamine (6.12 mL). This solution was then added to the above mixed anhydride at –78 ºC over 5 min. The mixture was stirred for 5 days at rt. The volatiles were removed *in vacuo* and the resultant white paste was redissolved in dichloromethane (200 mL) and 1 M NaOH (100 mL). The aqueous phase was separated and the organic phase was washed with brine, dried with sodium sulfate and removed of volatiles *in vacuo*. The residue was purified by flash chromatography to give compound **11** (13.90 g, 80% yield) as a colorless oil. **11:** R_f = 0.75 (50% EtOAc in hexane); $[\alpha]_D^{20}$ = +20.6° (*c* 0.63, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.35-7.19 (m, 10H), 5.10 (s, 1H), 4.99 (s, 1H), 4.66 (m, 1H), 4.50 (s, 2H), 4.16 (m, 2H), 3.99 (s, 2H), 3.29 (dd, *J* =13.3, 3.2 Hz, 1H), 2.96 (m, 2H), 2.75 (dd, *J* =13.3, 9.6 Hz, 1H), 2.20 (t, *J* = 7.6 Hz, 2H), 1.89 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.1, 153.5, 145.2, 138.4, 135.4, 129.5, 129.0, 128.4, 127.7, 127.6, 127.4, 112.4, 73.0, 72.0, 66.2, 55.2, 37.9, 35.1, 32.4, 22.1; IR (film, cm^{-1}): 2922, 2852, 1782, 1702, 1455, 1386, 1352, 1212, 1110, 1078; LRMS (EI): *m/z* 393 (M^+, 2), 302 (33), 287 (94), 232 (64), 219 (29), 178 (77), 91 (100); HRMS (EI): Calculated for $C_{24}H_{27}NO_4$: 393.1940; Found: 393.1943.

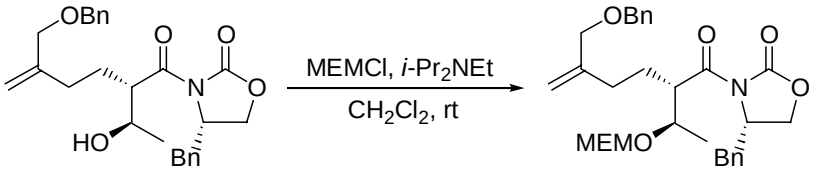
[4] Gage, J. R.; Evans, D. A. *Org. Synth.* **1990**, *68*, 77.

The basic aqueous phase was acidified and extracted with ethyl acetate. The organic phase was washed with brine, dried with sodium sulfate and concentrated *in vacuo*. The residue was purified by flash chromatography to recover acid **10'** (1.40 g, 18% yield).



11 **12**

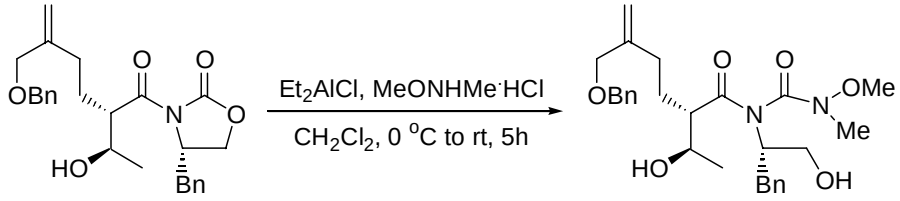
To a two-necked flask was added acylated oxazolidinone **11** (1.362 g, 3.466 mmol) and anhydrous dichloromethane (10 mL) under argon. The contents of the flask were cooled to 0 ºC. To this cooled solution was added dibutylboron triflate (4.16 mL, 4.16 mmol) followed by triethylamine (0.69 mL, 4.973 mmol) dropwise at such a rate as to keep the internal temperature below +3 ºC. The mixture was cooled to –78 ºC and acetaldehyde (0.22 mL, 3.936 mmol) was added slowly via syringe. The solution was stirred at –78 ºC for 20 min, then at 0 ºC for1 h. The reaction mixture was quenched by the addition of 12 mL of 2:1 methanol-30% aqueous hydrogen peroxide at such a rate as to keep the internal temperature below +10 ºC. After the solution was stirred for additional 1 h, the volatiles were removed and the resulting slurry was extracted with diethyl ether (3 x 20 mL). The combined organic extracts were washed with saturated sodium bicarbonate and brine, dried over magnesium sulfate and concentrated *in vacuo*. The residue was purified by flash chromatography to give recovered oxazolidinone **11** (0.367 g, 27% yield) and aldol adduct **12** (1.018 g, 67% yield) as a pale yellow oil. **12:** R_f = 0.40 (50% EtOAc in hexane); $[\alpha]_D^{20}$ = +23.1° (*c* 0.36, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.35-7.19 (m, 10H), 5.07 (s, 1H), 4.98 (s, 1H), 4.70 (m, 1H), 4.47 (s, 2H), 4.12 (m, 4H), 3.98 (s, 2H), 3.35 (dd, *J* =13.2, 3.1 Hz, 1H), 2.62 (dd, *J* = 13.2, 10.1 Hz, 1H), 2.52 (br s, 1H), 2.20-2.01 (m, 3H), 1.80 (m, 1H), 1.24 (d, *J* = 6.3 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 175.0, 153.9, 145.2, 138.2, 135.3, 129.4, 129.0, 128.4, 127.7, 127.6, 127.4, 112.7, 72.9, 72.0, 68.9, 66.1, 55.7, 48.4, 38.0, 31.0, 25.5, 19.5; IR (film, cm^{-1}): 3442, 2923, 2852, 1780, 1705, 1444, 1385, 1352, 1211, 1079; LRMS (FAB): *m/z* 438 (M^++1, 3), 420 (1), 330 (3), 307 (18), 154 (100), 136 (58), 107 (7), 91 (16), 77 (5).



12 **13**

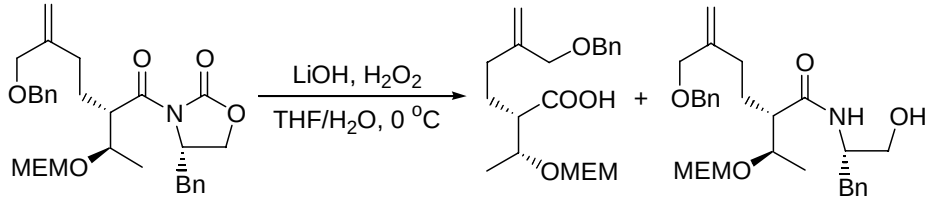
To a solution of compound **12** (2.07 g, 4.74 mmol) in dichloromethane (10 mL) was added diisopropylethylamine (1.75 mL, 10.07 mmol), followed by MEMCl (1.10 mL, 9.64 mmol) at room temperature under argon. After stirring for 4 h, water (10 mL) was added to the reaction mixture and the resulting oil was extracted with ether (3 x 30 mL). The combined organic layers were dried over sodium sulfate and concentrated *in vacuo*. The residue was purified by flash chromatography to afford compound **13**

(2.31 g, 93% yield) as a colorless oil. **13:** R_f = 0.48 (50% EtOAc in hexane); $[\alpha]_D^{20}$ = +18.3° (*c* 0.81, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.35-7.19 (m, 10H), 5.07 (s, 1H), 4.98 (s, 1H), 4.69 (s, 2H), 4.67 (m, 1H), 4.48 (s, 2H), 4.14 (m, 3H), 4.02 (t, *J* = 5.9 Hz 1H), 3.97 (s, 2H), 3.67 (m, 2H), 3.54 (m, 2H), 3.36 (s, 3H), 3.35 (dd, *J* = 13.2, 3.1 Hz, 1H), 2.64 (dd, *J* = 13.2, 10.2 Hz, 1H), 2.17-2.02 (m, 3H), 1.75 (m, 1H), 1.22 (d, *J* = 6.3 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.9, 153.3, 145.3, 138.3, 135.5, 129.4, 128.9, 128.4, 127.7, 127.6, 127.4, 112.4, 93.9, 73.6, 72.9, 72.0, 71.8, 67.1, 65.9, 59.0, 55.9, 47.1, 37.9, 31.0, 25.9, 17.3; IR (film, cm^{-1}): 2928, 2887, 1779, 1701, 1454, 1385, 1198, 1108, 1042; LRMS (EI): *m/z* 525 (M^+, 1), 450 (5), 358 (15), 330 (100), 304 (17), 178 (29), 91 (53), 89 (35); HRMS (EI): Calculated for $C_{30}H_{39}NO_7$: 525.2727, Found: 525.2726.



12 **12'**

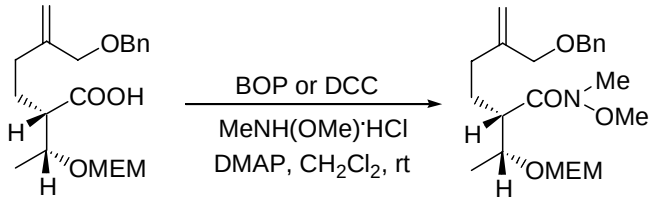
To a stirred suspension of MeONHMe·HCl (57 mg, 0.58 mmol) in CH_2Cl_2 (2 mL) was added 1.0 M Et_2AlCl in hexane (0.58 mL, 0.58 mmol) at 0 ºC. The mixture was allowed to warm to rt over 1 h. A solution of compound **12** (83 mg, 0.19 mmol) in CH_2Cl_2 (2 mL) was added dropwise. After stirring for 5 h, a solution of phosphate buffer (2 mL) was added. The mixture was diluted with $CHCl_3$, and filtered through a Celite pad. The celite was washed thoroughly with $CHCl_3$. The filtrate was extracted with $CHCl_3$. The combined organic layers were washed with brine, dried over $MgSO_4$ and concentrated. The residue was purified by silica gel flash chromatography to give compound **12'** (29 mg, 32% yield) as a colorless oil. **12':** R_f = 0.15 (60% EtOAc in hexane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.36-7.16 (m, 10H), 5.88 (br s, 1H), 5.07 (s, 1H), 4.97 (s, 1H), 4.48 (s, 2H), 4.42 (t, *J* = 8.1 Hz, 1H), 4.10 (m, 2H), 4.00 (m, 1H), 3.96 (s, 2H), 3.67 (s, 3H), 3.21 (m, 1H), 3.20 (s, 3H), 2.87 (m, 3H), 2.05 (m, 2H), 2.00-1.82 (m, 2H), 1.21 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.4, 145.5, 138.4, 136.0, 129.0, 128.98, 128.4, 127.7, 127.6, 127.2, 111.9, 73.0, 71.9, 69.6, 68.4, 61.5, 53.8, 46.1, 41.4, 32.0, 31.1, 24.4, 20.6; IR (film, cm^{-1}): 3512 (br) 2941, 2889, 1682, 1657, 1452, 1381, 1267, 1125, 1049; LRMS (EI): *m/z* 433 (M^+ – OMe – OH – OH, 3), 376 (21), 342 (12), 285 (17), 244 (27), 152 (29), 91 (100); HRMS (EI): Calculated for $C_{27}H_{33}N_2O_3$ (M^+ – OMe – OH – OH): 433.2491; Found: 433.2496.



13 **14** **16**

To a solution of compound **13** (220 mg, 0.419 mmol) in 5 mL of 4:1 THF-distilled water was added 50% aqueous hydrogen peroxide at 0 ºC under argon, followed by lithium hydroxide monohydrate (30 mg, 0.714 mmol) in 2 mL of distilled water. After stirring for 1 h, sodium sulfite (225 mg, 1.786 mmol) in 3 mL of distilled water was added. The bulk of the THF was removed on a rotary evaporator and the resulting mixture (pH 12-13) was extracted with dichloromethane (3 x 5 mL). The aqueous layer was cooled in an ice bath and acidified to pH 4. The resultant cloudy solution was extracted with ethyl acetate (3 x 5 mL). The combined ethyl acetate extracts were dried over anhydrous magnesium sulfate and concentrated *in vacuo* to afford the desired acid **14** (108 mg, 70% yield) as a pale yellow oil. **14:** R_f = 0.21 (50% EtOAc in hexane); $[\alpha]_D^{20}$ = +29.8° (*c* 1.72, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.34-7.27 (m, 5H), 5.08 (s, 1H), 4.97 (s, 1H), 4.78 (d, *J* = 7.2 Hz, 1H), 4.73 (d, *J* = 7.2 Hz, 1H), 4.49 (s, 2H), 3.98 (m, 1H), 3.96 (s, 2H), 3.70 (m, 2H), 3.54 (m, 2H), 3.38 (s, 3H), 2.58 (m, 1H), 2.15 (m, 2H), 1.82 (m, 2H), 1.24 (d, *J* = 6.3 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 178.7, 145.0, 138.2, 128.4, 127.7, 127.6, 112.6, 94.1, 73.9, 72.9, 71.9 71.7, 67.1, 59.0, 50.8, 31.1, 25.9, 17.6. IR (film, cm^{-1}): 3475 (br), 2975, 2932, 2867,1712, 1455, 1383, 1107, 1039; LRMS (EI): *m/z* 366 (M^+, 1), 291 (8), 247 (19), 232 (36), 170 (23), 141 (39), 91 (100), 89 (45). HRMS (EI): Calculated for $C_{20}H_{30}O_6$: 366.2042; Found: 366.2044.

The dichloromethane layer was dried with Na_2SO_4 and concentrated *in vacuo*. Purification of the residue by flash chromatography gave recovered chiral auxiliary (47 mg, 63%) and compound **16** (44 mg, 21% yield) as a colorless oil. **16:** R_f = 0.16 (50% EtOAc in hexane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.34-7.16 (m, 10H), 6.30 (d, *J* = 8.0 Hz, 1H); 5.03 (s, 1H), 4.86 (s, 1H), 4.72 (d, *J* = 7.0 Hz, 1H), 4.69 (d, *J* = 7.0 Hz, 1H), 4.47 (s, 2H), 4.26 (m, 1H), 3.91 (s, 2H), 3.75 (m, 1H), 3.65 (m, 3H), 3.53 (m, 3H), 3.36 (s, 3H), 3.10 (br s, 1H), 2.83 (m, 2H), 2.38 (m, 1H), 2.05-1.77 (m, 3H), 1.50 (m, 1H), 1.15 (d, *J* = 6.3 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.0, 145.2, 138.3, 137.8, 129.2, 128.5, 128.4, 127.7, 127.6, 126.5, 112.4, 95.0, 76.3, 72.9, 71.9, 71.8, 67.3, 64.1, 59.0, 52.5, 51.7, 37.0, 31.1, 26.3, 16.8. IR (film, cm^{-1}): 3440 (br) 2935, 2882, 1655, 1456, 1385, 1114, 1041, 909; LRMS (EI): *m/z* 393 (M^+ – MEM – OH, 9), 377 (15), 362 (21), 244 (33), 153 (21), 91 (100), 89 (47); HRMS (EI): Calculated for $C_{25}H_{31}NO_3$ (M^+ – MEM – OH): 393.2304; Found: 393.2301.

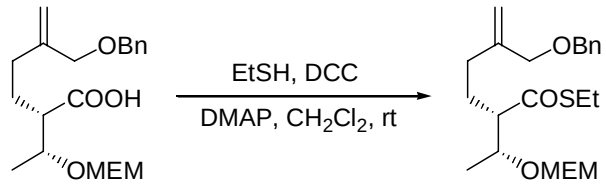


14 **14'**

The BOP method: To a solution of acid **14** (40 mg, 0.109 mmol) in CH_2Cl_2 (3 mL) was added *N,O*-dimethylhydroxylamine hydrochloride (14 mg, 0.144 mmol), Et_3N (0.052 mL, 0.375 mmol), and BOP (51 mg, 0.115 mmol) successively at rt. After stirring for 4 days, the mixture was diluted with CH_2Cl_2 (6 mL) and washed successively with 5% $KHSO_4$, 5% $NaHCO_3$ and saturated NaCl. The organic phase was dried

over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure to give compound **14'** (16 mg, 36% yield) as a colorless oil after flash chromatography.

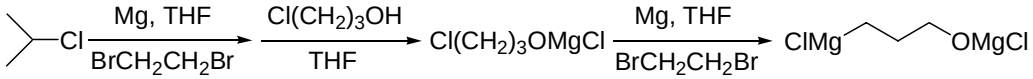
The DCC method: To a solution of **14** (40 mg, 0.109 mmol) in CH_2Cl_2 (3 mL) was added *N*,*O*-dimethylhydroxylamine hydrochloride (14 mg, 0.144 mmol), DIPEA (0.026 mL, 0.150 mmol), and DCC (25 mg, 0.121 mmol) successively at 0 ºC. After stirring for 3 days at rt, the DCU was filtered and washed with CH_2Cl_2 (1 mL). The organic solution was concentrated under reduced pressure. DCU precipitation in ether and filtration, followed by flash chromatography gave compound **14'** (20 mg, 44% yield) as a colorless oil. **14':** R_f = 0.35 (50% Et_2O in hexane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.34-7.25 (m, 5H), 5.06 (s, 1H), 4.95 (s, 1H), 4.79 (d, *J* = 7.1 Hz, 1H), 4.72 (d, *J* = 7.1 Hz, 1H), 4.47 (s, 2H), 3.95 (s, 2H), 3.90 (m, 1H), 3.69 (m, 2H), 3.67 (s, 3H), 3.53 (m, 2H), 3.37 (s, 3H), 3.18 (s, 3H), 3.04 (br m, 1H), 2.03 (m, 2H), 1.90 (t, *J* = 7.2 Hz, 2H), 1.19 (d, *J* = 6.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 175.1 (br), 145.6, 138.4, 111.7, 94.4, 74.9, 73.1, 71.9, 71.8, 67.1, 61.3, 59.1, 46.7, 32.2, 30.9, 27.2, 18.4; IR (film, cm^{-1}): 2935, 2884, 1657, 1455, 1385, 1112, 1040, 908; LRMS (EI): *m/z* 409 (M^+, 2), 378 (5), 349(9), 334 (14), 273 (28), 241 (25), 183 (23), 167 (29), 91 (100), 89 (65); HRMS (EI): Calculated for $C_{22}H_{35}NO_6$: 409.2464; Found: 409.2452.



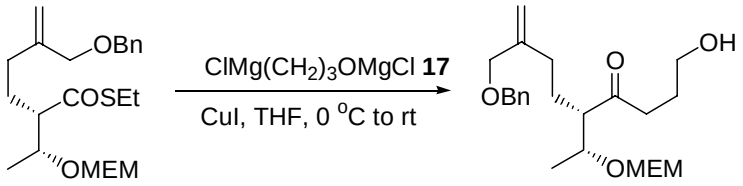
14 **15**

To a stirred solution of carboxylic acid **14** (0.770g, 2.104 mmol) in anhydrous CH_2Cl_2 (5 mL) was added DMAP (0.016 g, 0.130 mmol) and ethanethiol (0.31 mL, 4.145 mmol). DCC (0.530 g, 2.573 mmol) was added to the reaction mixture at 0 ºC, which was then stirred 3 h at room temperature. Precipitated DCU was then filtered off, and the filtrate was concentrated. The residue was taken up in CH_2Cl_2. The CH_2Cl_2 solution was washed twice with 0.5 N HCl, then with saturated $NaHCO_3$ and brine. The solution was dried over $MgSO_4$ and concentrated *in vacuo*. The residue was purified by flash chromatography on silica gel to afford thioester **15** (0.790 g, 91% yield) as a colorless oil. **15:** R_f = 0.82 (33% EtOAc in hexane); $[\alpha]_D^{20}$ = +36.7° (*c* 1.32, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.35-7.27 (m, 5H), 5.08 (s, 1H), 4.96 (s, 1H), 4.77 (d, *J* = 7.2 Hz, 1H), 4.71 (d, *J* = 7.2 Hz, 1H), 4.48 (s, 2H), 3.95 (s, 2H), 3.88 (m, 1H), 3.70 (m, 2H), 3.54 (m, 2H), 3.38 (s, 3H), 2.88 (q, *J* = 7.4 Hz, 2H), 2.70 (m, 1H), 2.10 (m, 2H), 1.86 (m, 2H), 1.82 (m, 3H), 1.24 (t, *J* = 7.4 Hz, 3H), 1.20 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 201.0, 145.2, 138.4, 128.3, 127.7, 127.5, 112.3, 94.2, 74.3, 73.0, 71.9, 71.7, 67.1, 59.7, 59.0, 30.7, 27.0, 23.4, 18.2, 14.7; IR (film, cm^{-1}): 2973, 2930, 2882, 1682, 1454, 1458, 1248, 1078, 1036, 906, 820; LRMS (EI): *m/z* 321 (M^+ - MEM, 5), 273 (15), 215 (24), 153 (22), 91 (100), 89 (36); HRMS (EI): Calculated for $C_{22}H_{34}O_5S$ (M^+ - MEM): 321.1534; Found: 321.1528.

Preparation of Grignard reagent 17[5]



To a 25 mL two neck round bottom flask fitted with a condenser was added magnesium turnings (0.18 g, 7.5 mmol), THF (5 mL) and 1, 2-dibromoethane (0.025 mL). Isopropyl chloride (0.46 mL, 5.0 mmol) was added slowly at room temperature. The reaction mixture was stirred vigorously and heated to reflux for 2 h. After cooling to room temperature, the Grignard reagent solution was transferred via cannula to another flask containing 3-chloropropanol (0.43 mL, 5.0 mmol) and dry THF (5 mL) at –20 ºC. After stirring for further 20 minutes, magnesium turnings (0.18 g, 7.5 mmol) and 1,2-dibromoethane (0.025 mL) were added to this solution. The resultant mixture was heated to reflux for 2 h and cooled to room temperature to give a solution Grignard reagent **17**.

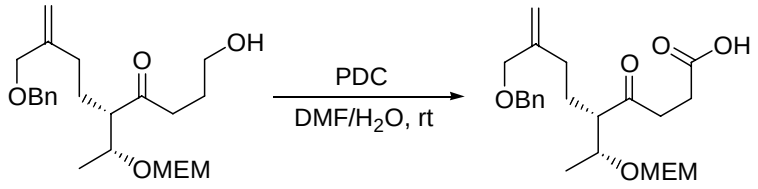


15 **18**

The Grignard reagent $ClMg(CH_2)_3OMgCl$ **17** (10 mL, 5 mmol) was transferred into a flask containing thioester **15** (0.680g, 1.659 mmol), CuI (1.43 g, 7.5 mmol), Me_2S (1.20 mL) in THF (10 mL) under argon at 0 ºC. The resultant mixture was stirred at room temperature overnight and quenched with saturated NH_4Cl. The organic layer was separated and the aqueous layer was extracted with ethyl acetate (3 x 20 mL). The combined organic phases were washed with brine, dried over $MgSO_4$ and evaporated under reduced pressure. The residue was purified by flash chromatography to give alcohol **18** (0.52 g, 77% yield) as a colorless oil. **18:** R_f = 0.25 (67% EtOAc in hexane); [α] = +17.5° (*c* 0.76, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.37-7.25 (m, 5H), 5.06 (s, 1H), 4.93 (s, 1H), 4.76 (d, *J* = 7.1 Hz, 1H), 4.71 (d, *J* = 7.1 Hz, 1H), 4.47 (s, 2H), 3.93 (s, 2H), 3.90 (m, 1H), 3.69 (m, 2H), 3.56 (m, 4H), 3.39 (s, 3H), 2.78 (m, 2H), 2.52 (dt, J = 18.3, 6.6 Hz,1H), 2.26 (br s, 1H), 2.00 (m, 2H), 1.82 (m, 3H), 1.62 (m, 1H), 1.11 (d, *J* = 6.3 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 212.9, 145.3, 138.2, 128.4, 127.7, 127.6, 112.5, 93.9, 74.1, 72.9, 72.0, 71.7, 67.2, 61.9, 59.0, 56.7, 41.5, 31.1, 26.0, 25.9, 17.3; IR (film, cm^{-1}): 3480 (br), 1708, 1454, 1375, 1245, 1097, 1042; LRMS (EI): *m/z* 302 (M^+ – MEM – OH, 4), 375 (2), 301 (4), 284 (18), 257 (15), 195 (37), 193 (70), 174 (40), 91 (100), 89 (64); HRMS (EI): Calculated for $C_{19}H_{26}O_3$ (M^+ – MEM – OH): 302.1882; Found: 302.1880.

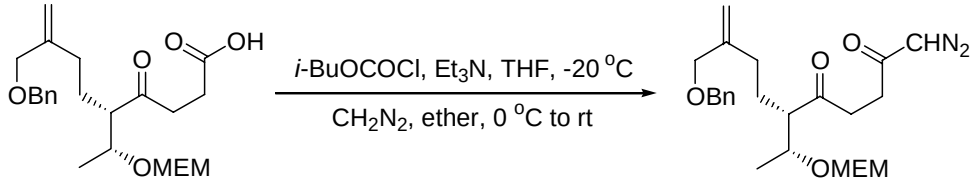
Unreacted thioester **15** (116 mg, 17%) was recovered in the reaction.

[5] Normant, J. F.; Cahiez, G.; Alexakis, A. *Tetrahedron Lett.* **1978**, *33*, 3013.



18 **19**

Alcohol **18** (88 mg, 0.216 mmol) in DMF/H_2O (1 ml/0.025 mL) was treated with PDC (0.49 g, 1.293 mmol) at room temperature for 8 h. Water (20 mL) was then added and the mixture was extracted with EtOAc (5 x 5 mL). The combined organic extracts were dried over $MgSO_4$ and concentrated *in vacuo*. The residue was purified by flash chromatography to afford compound **19** (67 mg, 75% yield) as a colorless oil. **19:** R_f = 0.18 (75% EtOAc in hexane); $[\alpha]_D^{20}$ = +24.1° (*c* 0.69, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.77 (br s, 1H), 7.37-7.25 (m, 5H), 5.06 (s, 1H), 4.93 (s, 1H), 4.76 (d, *J* = 7.1 Hz, 1H), 4.71 (d, *J* = 7.1 Hz, 1H), 4.47 (s, 2H), 3.93 (s, 2H), 3.88 (m, 1H), 3.68 (m, 2H), 3.54 (m, 2H), 3.38 (s, 3H), 2.88 (m, 1H), 2.72 (m, 2H), 2.57 (m, 2H), 2.02 (m, 2H), 1.90 (m, 1H), 1.62 (m, 1H), 1.11 (d, *J* = 6.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 210.3, 177.9, 145.2, 138.2, 128.3, 127.7, 127.5, 112.4, 93.9, 74.0, 72.8, 71.9, 71.7, 67.1, 59.0, 56.4, 39.3, 31.0, 27.5, 25.9, 17.1; IR (film, cm^{-1}): 3502, 2930, 1712, 1456, 1384, 1112, 1040; LRMS (EI): *m/z* 333 (M^+ – MEM, 6), 391 (5), 347 (9), 242 (28), 197 (31), 91 (100), 89 (52); HRMS (EI): Calculated for $C_{19}H_{25}O_5$ (M^+ – MEM) 333.1702; Found: 333.1699.

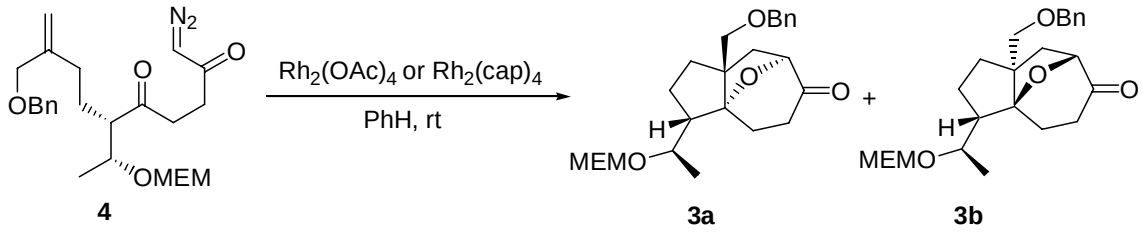


19 **4**

Diazomethane was prepared as described in the literature.[6]

Acid **19** (120 mg, 0.294 mmol) in a solution of dry ether (2 mL) and THF (2 mL) was stirred at –20 ºC under argon. To this solution, triethylamine (0.061 mL, 0.439 mmol) followed by isobutyl chloroformate (0.057 mL, 0.440 mmol) were added. The solution was stirred for 30 min and allowed to warm to 0 ºC. At this temperature ethereal diazomethane (3 mL, about 1.0 mmol) was added dropwise. The cooling bath was removed and the reaction mixture was stirred for a further 3 h. It was evaporated to a third of its original volume. The solution was diluted with ether (10 mL) and washed with water, saturated aqueous sodium bicarbonate, and brine. It was dried with sodium sulfate and concentrated *in vacuo*. The residue was purified by flash chromatography to give the diazoketone was **4** (89 mg, 72% yield) as a yellow oil. **4:** R_f = 0.23 (40% EtOAc in hexane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.37-7.27 (m, 5H), 5.28 (br s, 1H), 5.07 (s, 1H), 4.94 (s, 1H), 4.76 (d, *J* = 7.1 Hz, 1H), 4.71 (d, *J* = 7.1 Hz, 1H), 4.48 (s, 2H), 3.94 (s, 2H), 3.88 (m, 1H), 3.68 (m, 2H), 3.54 (m, 2H), 3.38 (s, 3H), 2.95 (dt, *J* = 18.9, 6.4 Hz, 1H), 2.78 (m, 2H), 2.55 (br m, 2H), 2.01 (m, 2H), 1.86 (m, 1H), 1.60 (m, 1H), 1.11 (d, *J* = 6.3 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 210.9, 193.4, 145.3,

138.4, 128.4, 127.7, 127.6, 112.4, 94.0, 74.1, 72.9, 72.0, 71.7, 67.2, 59.1, 56.5, 54.5 (br), 39.4 (br), 33.9 (br), 31.1, 26.1, 17.2; IR (film, cm^{-1}): 2929, 2896, 2108, 1711, 1644, 1380, 1100, 1039.



4 **3a** **3b**

A solution of diazoketone **4** (50 mg, 0.112 mmol) in dry benzene (10 mL) was treated with $Rh_2(OAc)_4$ (0.5 mg, 1.13 x 10^{-3} mmol) at room temperature for 6 h. The reaction mixture was filtered and concentrated under reduced pressure. The crude oil was purified by flash chromatography on silica gel to give product **3** (31 mg, 66 % yield, **3a** : **3b** = 1.25:1).

A solution of diazoketone **4** (30 mg, 0.0673 mmol) in dry benzene (5 mL) was treated with $Rh_2(cap)_4$ (0.5 mg, 7.65 x 10^{-4} mmol) for 24 h at room temperature. The reaction mixture was filtered and concentrated under reduced pressure. The crude oil was purified by flash chromatography on silica gel to give product **3** (19.4 mg, 69 % yield, **3a : 3b** = 1.1:1).

Data for the mixture of **3a** + **3b**: R_f = 0.48 (40% EtOAc in hexane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.37-7.27 (m, 5H), 4.77 (s, 0.56 x 2H), 4.58 (q-AB, 0.44 x 2H), 4.50 (s, 0.44 x 2H), 4.48 (s, 0.56 x 2H), 4.31 (m, 1H), 4.03 (m, 0.56 x 1H), 3.87 (m, 0.44 x 1H), 3.80-3.47 (m, 5H), 3.383 (s, 0.56 x 3H), 3.379 (s, 0.44 x 3H), 3.29 (q-AB, 0.56 x 2H), 2.66-1.55 (m, 11H), 1.29 (d, *J* = 6.4Hz, 0.56 x 3H), 1.19 (d, *J* = 6.3 Hz, 0.44 x 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (212.12, 209.62), (138.20, 137.80), 128.4, 127.75, 127.69, 127.62, 94.70, 94.15, 92.34, (82.42, 82.36), 74.21, (73.13, 72.04), (71.84, 71.78), (67.49, 66.96), (59.09, 59.05), (56.20, 56.16), (53.82, 52.54), (42.08, 40.56), (37.74, 36.37), (33.67, 33.13), (29.70, 25.88), (24.83, 24.67), (20.57, 19.30); IR (film, cm^{-1}): 2934, 2874, 1728, 1455, 1364, 1103, 1037; LRMS (EI): *m/z* 418 (M^+, 2), 342 (20), 329 (9) 299 (12), 221 (45),111(44), 89 (100). HRMS (EI): Calculated for $C_{24}H_{34}O_6$: 418.2355; Found: 418.2360.

Careful separation of the mixture of **3a** + **3b** by column chromatography gave an analytically pure sample of **3b**. **3b:** $[\alpha]_D^{20}$ = –26.3° (*c* 0.11, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.37-7.27 (m, 5H), 4.60 (d, *J* = 7.0 Hz, 1H), 4.57 (d, *J* = 7.1 Hz, 1H), 4.50 (s, 2H), 4.32 (br d, *J* = 6.6 Hz, 1H), 3.87 (dq, *J* = 6.3, 2.2Hz, 1H), 3.62 (m, 1H), 3.53 (q, *J* = 4.1 Hz, 1H), 3.50 (s, 2H), 3.48 (d, *J* = 9.2 Hz, 1H), 3.46 (d, *J* = 9.2 Hz, 1H), 3.38 (s, 3H), 2.61 (dt, J = 17.7, 8.9 Hz, 1H), 2.36 (m, 1H), 2.22 (m, 1H), 2.18 (m, 2H), 2.12 (m, 1H), 2.01 (m, 1H), 1.91 (m, 3H), 1.66 (m, 1H), 1.19 (d, *J* = 6.3 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 209.6, 138.2, 128,4, 127.7, 127.7, 94.7, 94.2, 82.4, 73.5, 73.1, 71.8, 71.4, 67.5, 59.1, 56.2, 53.8, 40.6, 37.7, 33.1, 25.9, 24.3, 19.3; IR (CH_2Cl_2, cm^{-1}): 2935, 2874, 1728, 1456, 1362, 1103, 1035; LRMS (EI): *m/z* 418 (M^+, 2), 342 (16), 329 (11) 299 (15), 221 (36),111 (49), 89 (100). HRMS (EI): Calculated for $C_{24}H_{34}O_6$: 418.2355; Found: 418.2360.

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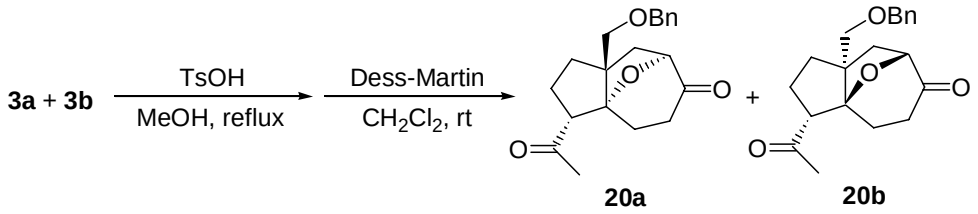
[6] (a) De Boer, Th. J.; Backer, H. J. *Org. Synth. Coll. Vol 4*, **1963**, 250. (b) Hudlicky, M. *J. Org. Chem.* **1980**, *45*,

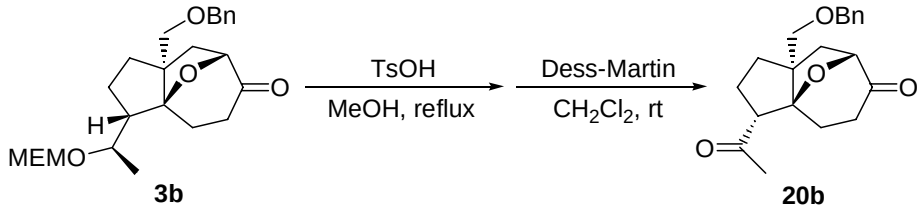
3a could not be obtained pure by chromatography.



To a solution of **3a** + **3b** (40 mg, 0.096 mmol) in MeOH (3 mL) was added TsOH (37 mg, 0.20 mmol). The mixture was heated to reflux for 1h. MeOH was removed under reduced pressure and EtOAc (5 mL) was added. The resulting solution was washed with saturated $NaHCO_3$ and brine. The organic layer was dried with Na_2SO_4 and concentrated *in vacuo*. The crude product was purified by flash chromatography to afford the alcohols (25 mg, 80%) as a colorless oil.

To the alcohols (25 mg, 0.076 mmol) in dry CH_2Cl_2 (1 mL) was added the Dess-Martin reagent[7] (50 mg, 0.12 mmol) at room temperature. After stirring for 6 h, saturated $Na_2S_2O_3$ solution was added dropwise to the reaction mixture until it turned clear. Saturated $NaHCO_3$ was added and the solution was extracted with EtOAc (3 x 5 mL). The combined organic extracts were dried with Na_2SO_4 and concentrated *in vacuo*. The crude product was purified by flash chromatography to afford **20a** and **20b** (23 mg, 93%, **20a** : **20b** = 1:1.25) as a colorless oil.

Careful separation of the mixture of **20a** + **20b** by column chromatography gave a pure sample of **20a** for analytical purpose. **20a**: $[\alpha]_D^{20}$ = +13.6° (*c* 0.13, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.38-7.27 (m, 5H), 4.48 (s, 2H), 4.37 (dd, *J* = 5.3, 4.2 Hz, 1H), 3.33 (d, *J* = 9.5 Hz, 1H), 3.27 (d, *J* = 9.5 Hz, 1H), 2.60 (dd, *J* = 11.8, 6.4 Hz, 1H), 2.47-2.29 (m, 4H), 2.25 (s, 3H), 2.042 (d, *J* = 5.5 Hz, 1H), 2.039 (d, *J* = 4.0 Hz, 1H), 1.90 (m, 3H), 1.72 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 211.4, 209.2, 137.5, 128.5, 127.9, 127.6, 92.7, 82.7, 73.6, 73.5, 60.1, 55.3, 42.0, 36.6, 33.6, 30.3, 26.3, 23.9; IR (CH_2Cl_2, cm^{-1}): 2960, 2929, 2865, 1726, 1695, 1455, 1358, 1104, 1076, 1030; LRMS (EI): *m/z* 328 (M^+, 23), 237 (33), 194 (100), 179 (45), 149 (60); HRMS (EI): Calculated for $C_{20}H_{24}O_4$: 328.1675; Found: 328.1670.



20b was prepared from pure **3b** by the same method used above for the synthesis of **20a+20b** from **3a+3b**. **20b:** $[\alpha]_D^{20}$ = –22.9° (*c* 0.18, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.38-7.27 (m, 5H), 4.52 (d, *J* = 12.1 Hz, 1H), 4.46 (d, *J* = 12.1 Hz, 1H), 4.30 (d, *J* = 7.4 Hz, 1H), 3.62 (d, *J* = 9.2 Hz, 1H), 3.44 (d, *J* = 9.2 Hz, 1H), 3.33 (dd, *J* = 8.3, 2.2 Hz, 1H), 2.38 (m, 3H), 2.25 (m, 1H), 2.21 (s, 3H), 2.15 (q, *J* = 6.9 Hz, 1H),

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[7] Boeckman Jr., R. K.; Shao, P.; Mullins, J. J. *Org. Synth*. **1999**, *77*, 141.

2.03 (dd, *J* = 8.8, 6.9 Hz, 1H), 1.98 (dd, *J* = 12.8, 8.3 Hz, 1H), 1.83 (ddd, *J* = 6.6, 3.7, 2.5 Hz, 1H), 1.72 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 211.7, 209.5, 137.9, 128.4, 127.8, 127.6, 93.3, 82.4, 73.4, 72.5, 61.5, 54.9, 42.0, 37.9, 33.8, 31.2, 27.2, 24.6; IR (CH_2Cl_2, cm^{-1}): 2958, 2938, 2869, 1726, 1709, 1455, 1364, 1104, 1088, 1028; LRMS (EI): *m/z* 328 (M^+, 19), 237 (26), 194 (100), 179 (53), 149 (67); HRMS (EI): Calculated for $C_{20}H_{24}O_4$: 328.1675; Found: 328.1672.