Asymmetric Total Synthesis and Formal Total Synthesis of the Antitumor Sesquiterpenoid (+)-Eremantholide A

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Supporting Information

Part 1. Experimental Procedures

General Methods

Reaction solvents (THF, PhMe, C₆H₆, CH₂Cl₂) were freshly distilled from freshly activated 4Å molecular sieve beads under a N₂ atmosphere prior to use. Cyclohexanone, EtOAc and Petrol 40-60 °C were distilled prior to use. MeOH was distilled from Mg metal under a N₂ atmosphere prior to use. All 500 MHz ¹H NMR spectral data that are reported in CDCl₃ are referenced relative to the residual CHCl₃ peak at δ 7.24, and all data that are reported in C₆D₆ are referenced with respect to the residual C₆H₆ peak at δ 7.15. For the 125 MHz ¹³C NMR data that are reported in CDCl₃, the triplet at δ 77.00 is used as the reference peak, whilst for spectra recorded in C₆D₆, the triplet centred at δ 128.00 is the reference peak. Unless otherwise specified, all IR spectra were recorded as neat films on NaCl plates.

Experimental Procedures for the Asymmetric Total Synthesis of (+)-Eremantholide A

Please Note: For our NMR assignments, we have used (+)-eremantholide A numbering throughout.

Oxazolidinone **13** (II-YL-105)

To a stirred solution of oxazolidinone **40** (35.5 g, 0.2 mol) in dry THF (250 mL) at -78 °C under N₂ was added *n*-BuLi (2.5 M solution in hexanes, 84 mL, 0.21 mol, 1.05 equiv) dropwise over 0.5 h. The resulting bright orange solution was stirred at -78 °C for a further 5 min, whereafter 4-pentenoyl chloride (26.5 mL, 0.24 mol) was added dropwise over 20 min. The reactants were stirred at -78 °C for 0.5 h and the cooling bath was removed. After warming the reaction mixture to rt, it was quenched with saturated aqueous NH₄Cl (500 mL). After separation of the organic layer, the aqueous phase was extracted with Et₂O (3 x 1L). The combined organic layers were washed with H₂O (500 mL), brine (200 mL), dried over MgSO₄, filtered, and concentrated in *vacuo*. Recrystallisation of the crude residue from petrol (40-60 °C) gave oxazolidinone **13** (44.5 g, 86%) as white crystals.

Data for **13**: [α]_D +38.6 ° (*c* 0.684, CH₂Cl₂); IR (KBr) 3071 (w), 2989 (w), 2939 (w), 1776 (s), 1699 (s), 1643 (w), 1454 (m), 1352 (s), 1277 (m), 1196 (s), 1155 (m), 1124 (m), 1039 (m), 991 (m), 914 (m), 766 (m), 698 (m) cm⁻¹; ¹H NMR (500 MHz, CDCl₃, 298K) δ 7.44-7.24 (m, 5H, Ph), 5.82 (m, 1H, H-12), 5.63 (d, 1H, *J* = 7.3 Hz, PhCH(O)-), 5.06 (m, 1H, H-12'b), 4.99 (dd, 1H, *J* = 1.1, 10.2 Hz, H-12'a), 4.73 (m, 1H, MeCH(N)-), 3.07 (dt, 1H, *J* = 7.3, -17.2 Hz, H-7a), 2.97 (dt, 1H, *J* = 7.4, -17.1 Hz, H-7b), 2.42 (m, 1H, H-11a), 2.39 (m, 1H, H-11b), 0.86 (d, 3H, *J* = 6.6 Hz, MeCH(N)-) ppm; ¹³C NMR (125 MHz, CDCl₃, 298K) δ 172.18 (C-6 C=O), 152.94 (-N(C=O)O-), 136.59 (C-12), 133.24 (q C of Ph), 128.65 (Ph), 128.60 (Ph), 125.55 (Ph), 115.58 (C-12'), 78.90 (PhCH(O)-), 54.63 (MeCH(N)-), 34.79 (C-7), 28.14 (C-11), 14.48 (Me) ppm; VG 70-SE Positive ion FAB HRMS: Calcd. for C₁₅H₁₇NNaO₃ (M+Na)⁺: 282.11061. Found: 282.11104.

Aldol Adduct **12** (II-YL-101)

Data for **12**: [α]_D -1.7 ° (c 0.648, CH₂Cl₂); IR 3512 (b r w), 3071 (w), 2934 (m), 2860 (w), 1782 (s), 1695 (m), 1639 (w), 1462 (w), 1425 (w), 1344 (s), 1194 (s), 1115 (s), 1069 (m), 1036 (w), 997 (w), 920 (w), 889 (w), 820 (w), 768 (w), 702 (s), 613 (w) cm⁻¹; ¹H NMR (500 MHz, CDCl₃, 298K) δ 7.71-7.66 (m, 4H, Ph), 7.47-7.33 (m, 9H, Ph), 7.29-7.25 (m, 2H, Ph), 5.85 (m, 1H, H-12), 5.44 (d, 1H, *J* = 7.2 Hz, PhCH(O)-), 5.03 (m, 1H, H-12'b), 4.98 (m, 1H, H-12a), 4.67 (m, 1H, MeCH(N)-), 4.33 (m, 1H, H-7), 4.10 (br dd, 1H, H-8), 3.79 (dd, 1H, *J* = 4.6, 10.4 Hz, H-9a), 3.75 (dd, 1H, *J* = 6.0, 10.4 Hz, H-9b), 2.79 (br s, 1H, OH), 2.55 (m, 2H, H-11a, H-11b), 1.10 (s, 9H, -C(Me)₃), 0.82 (d, 3H, *J* = 6.6 Hz, MeCH(N)-) ppm; ¹³C NMR (125 MHz, CDCl₃, 298K) δ 174.07 (C-6 C=O), 152.45 (-N(C=O)O-), 135.52 (Ph), 135.48 (Ph), 134.80 (C-12), 133.16 (q C of Ph), 133.01 (q C of Ph), 132.92 (q C of Ph), 129.79 (Ph), 129.78 (Ph), 128.66 (Ph), 128.61 (Ph), 127.73 (Ph), 125.50 (Ph), 117.19 (C-12'), 78.46 (PhCH(O)-), 71.78 (C-8), 65.40 (C-9), 54.79 (MeCH(N)-), 44.39 (C-7), 32.46 (C-11), 26.79 (-C(Me)₃), 19.14 (-C(Me)₃), 14.44 (Me) ppm; VG 70-SE Positive Ion FAB HRMS: Calcd. for C₃₃H₃₉NNaO₅Si (M+Na)⁺: 580.24951. Found: 580.24990.

Add LiBH_4 (1.5 equiv) over 0.5 h to **12** in MeOH (1.5 equiv), THF, 0 °C, stir 0.5 h (94%)

12

15

4

mL), separated, and dried over MgSO_4 . After filtration, and concentration *in vacuo*, the crude residue was purified by SiO_2 flash chromatography (gradient elution 10:1 to 2:1 petrol:EtOAc) to give **15** (39.2 g, 94%) as an oil.

Data for **15**: $[\alpha]_D -2.65^\circ$ (*c* 0.642, CH_2Cl_2); IR 3385 (br w), 3071 (w), 3932 (w), 2860 (w), 1468 (w), 1427 (w), 1389 (w), 1362 (w), 1109 (s), 1040 (w), 1003 (w), 914 (w), 793 (w), 702 (s), 741 (w), 613 (m) cm^{-1} ; ^1H NMR (500 MHz, CDCl_3 , 298K) δ 7.73-7.62 (m, 4H, Ph), 7.48-7.33 (m, 6H, Ph), 5.75 (m, 1H, H-12), 5.00 (m, 1H, H-12'b), 4.98 (m, 1H, H-12'a), 3.97 (m, 1H, H-8), 3.74 (dd, 1H, $J = 7.4, 10.4$ Hz, H-9a), 3.71 (m, 1H, H-9b), 3.69 (dd, 1H, $J = 6.1, 10.9$ Hz, H-6a), 3.64 (dd, 1H, $J = 4.0, 11.0$ Hz, H-6b), 2.85 (br s, 2H, OH-6 and OH-8), 2.11 (m, 2H, H-11a, H-11b), 1.84 (m, 1H, H-7), 1.09 (s, 9H, $-\text{C}(\text{Me})_3$) ppm; ^{13}C NMR (125 MHz, CDCl_3 , 298K) δ 135.76 (C-12), 135.46 (Ph), 135.44 (Ph), 132.93 (q C of Ph), 132.89 (q C of Ph), 129.83 (Ph), 129.81 (Ph), 127.76 (Ph), 127.75 (Ph), 116.36 (C-12'), 73.83 (C-8), 65.32 (C-9), 63.53 (C-6), 41.90 (C-7), 30.40 (C-11), 26.78 ($-\text{C}(\text{Me})_3$), 19.13 ($-\text{C}(\text{Me})_3$) ppm; VG 70-SE Positive Ion FAB HRMS: Calcd. for $\text{C}_{23}\text{H}_{32}\text{NaO}_3\text{Si}$ ($\text{M}+\text{Na}$) $^+$: 407.20183. Found: 407.20203.

Triol **16** (II-YL-47)

To diol **15** (40.1 g, 0.104 mol) and KF (9.1 g, 0.157 mol) was successively added DMF (200 mL) and H_2O (18.7 mL, 1.04 mol) and the mixture was heated at 50°C for 5 h. TLC analysis thereafter indicated that no starting material remained. The solvents were removed *in vacuo* and the crude residue was suspended in CH_2Cl_2 and the suspension loaded onto a SiO_2 flash chromatographic column. Elution of the column with neat CH_2Cl_2 followed by CH_2Cl_2 :MeOH (1:2) gave triol **16** (11.4 g, 75%) as a thick oil that solidified upon standing.

Data for **16**: $[\alpha]_D +6.16^\circ$ (*c* 0.406, MeOH); IR (KBr) 3352 (very br s), 3078 (m), 2930 (s), 2889 (s), 1641 (m), 1441 (s), 1418 (s), 1340 (br), 1213 (w), 1034 (s), 916 (s), 866 (w), 829 (w), 635 (m) cm^{-1} ; ^1H NMR (500 MHz, CDCl_3 , 298K) δ 5.74 (m, 1H, H-12), 5.03 (m, 1H, H-12'b), 5.00 (m, 1H, H-12'a), 4.29 (s, 3H, C-9-OH, C-8-OH, C-6-OH), 3.80 (m, 1H, H-8), 3.64 (dd, 1H, $J = 3.8, 11.0$ Hz, H-6a), 3.61 (m, 2H, H-9a, H-9b), 3.56 (dd, 1H, $J = 7.2, 11.1$ Hz, H-6b), 2.12 (m, 1H, H-11a), 2.02 (m, 1H, H-11b), 1.73 (m, 1H, H-7) ppm; ^{13}C NMR (125 MHz, CDCl_3 , 298K) δ 136.57 (C-12), 116.62 (C-12'), 72.90 (C-8), 64.11 (C-9), 61.96 (C-6), 42.86 (C-7), 31.05 (C-11) ppm; Electrospray HRMS: Calcd. for $\text{C}_7\text{H}_{15}\text{O}_3$ ($\text{M}+\text{H}$) $^+$: 147.10212. Found: 147.10194.

Cyclohexylidene Acetal **17** (II-YL-53)

Triol **16** (13.5 g, 92.35 mmol), cyclohexanone (95.7 mL, 0.9235 mol, 10 equiv), and *p*-TsOH (1.75 g, 9.2 mmol) were mixed together at rt under N₂ and EtOAc (500 mL) was added. The reactants were stirred at rt for 12 h and thereafter quenched with 0.1 N aqueous NaOH solution (50 mL). The organic layer was separated, washed with H₂O (50 mL), dried (MgSO₄), filtered, and concentrated *in vacuo* (the majority of excess cyclohexanone was best removed under high vacuum conditions). The residue was purified by SiO₂ flash chromatography (gradient elution from 10:1 to 3:1 petrol:EtOAc) to give alcohol **17** (15.6 g, 75%) as a colorless oil.

Data for **17**: [α]_D +1.17 ° (*c* 1.026, CH₂Cl₂); IR 3445 (br m), 3074 (w), 2936 (s), 2860 (m), 1638 (w), 1443 (w), 1366 (w), 1337 (w), 1281 (w), 1232 (w), 1163 (m), 1103 (s), 1040 (s), 1001 (w), 928 (m), 845 (w) cm⁻¹; ¹H NMR (500 MHz, CDCl₃, 298K) δ 5.69 (m, 1H, H-12), 4.94 (m, 1H, H-12'b), 4.90 (m, 1H, H-12'a), 4.04 (dd, 1H, *J* = 6.3, 13.9 Hz, H-8), 3.89 (dd, 1H, *J* = 6.2, 8.2 Hz, H-9a), 3.59 (dd, 1H, *J* = 7.9, 8.0 Hz, H-9b), 3.47 (m, 2H, H-6a, H-6b), 2.92 (br s, 1H, OH-6), 2.11 (m, 1H, H-11a), 1.99 (m, 1H, H-11b), 1.73 (m, 1H, H-7), 1.56-1.36 (m, 8 H, cyclohex), 1.35-1.19 (m, 2H, cyclohex) ppm; ¹³C NMR (125 MHz, CDCl₃, 298K) δ 136.09 (C-12), 116.29 (C-12'), 108.69 (-O-C-O-), 76.69 (C-8), 66.49 (C-9), 62.22 (C-6), 42.64 (C-7), 35.92 (cyclohex), 34.55 (cyclohex), 31.64 (C-11), 24.90 (cyclohex), 23.73 (cyclohex), 23.54 (cyclohex) ppm; VG 70-SE Positive Ion FAB HRMS: Calcd. for C₁₃H₂₂NaO₃ (M+Na)⁺: 249.14666. Found: 249.14687.

O-Benzoyl **18** (II-YL-61)

To a 0 °C solution of **17** (12.1 g, 53.5 mmol) in dry pyridine (200 mL) under N₂ was added benzoyl chloride (8.1 mL, 69.78 mmol) dropwise over 10 min. The mixture was stirred at 0 °C for 1 h and allowed to warm to rt where it was stirred for a further 3 h. After quenching with MeOH (2 mL) concentration *in vacuo* furnished a residue that was co-evaporated with PhMe (40 mL) several times to remove residual pyridine. The residue was purified by SiO₂ flash chromatography with petrol:Et₂O (7:1) to give **18** as a colorless oil (17.2 g, 97%).

Data for **18**: $[\alpha]_D +5.1^\circ$ (c 1.05, CH_2Cl_2); IR 3071 (w), 2937 (s), 2860 (w), 1722 (s), 1641 (w), 1603 (w), 1448 (w), 1367 (w), 1313 (w), 1273 (s), 1167 (w), 1107 (s), 1070 (w), 1034 (w), 995 (w), 930 (w), 712 (s) cm^{-1} ; ^1H NMR (500 MHz, CDCl_3 , 298K) δ 7.99 (m, 2H, Ph), 7.54 (m, 1H, Ph), 7.42 (m, 2H, Ph), 5.84 (m, 1H, H-12), 5.09 (m, 1H, H-12'b), 5.05 (m, 1H, H-12'a), 4.35 (dd, 1H, $J = 4.7, 11.4$ Hz, H-6a), 4.20 (dd, 1H, $J = 6.7, 11.4$ Hz, H-6b), 4.10 (dd, 1H, $J = 7.0, 13.3$ Hz, H-8), 4.08 (dd, 1H, $J = 6.0, 13.3$ Hz, H-9a), 3.73 (dd, 1H, $J = 7.1, 7.3$ Hz, H-9b), 2.47 (m, 1H, H-11a), 2.24 (m, 1H, H-11b), 2.07 (m, 1H, H-7), 1.70-1.46 (m, 8 H, cyclohex), 1.45-1.30 (m, 2H, cyclohex) ppm; ^{13}C NMR (125 MHz, CDCl_3 , 298K) δ 166.34 (C=O), 135.52 (C-12), 133.02 (Ph), 130.00 (Ph), 129.50 (Ph), 128.40 (Ph), 117.23 (C-12'), 109.11 (-O-C-O-), 76.21 (C-8), 67.70 (C-9), 64.48 (C-6), 41.13 (C-7), 36.26 (cyclohex), 35.04 (cyclohex), 32.49 (C-11), 25.15 (cyclohex), 23.97 (cyclohex), 23.84 (cyclohex) ppm; VG 70-SE Positive Ion FAB HRMS: Calcd. for $\text{C}_{20}\text{H}_{26}\text{NaO}_4$ ($\text{M}+\text{Na}$) $^+$: 353.17287. Found: 353.17187.

Alcohol **19** (II-YL-158)

Alkene **18** (13.1 g, 39.65 mmol) was dissolved in a mixture of $\text{MeOH}:\text{CH}_2\text{Cl}_2$ (2:1, 900 mL) in a 2 L round-bottomed flask, and the solution was cooled to -78°C . Ozone was continuously bubbled through the initially colorless reaction mixture until the color of the solution became blue. After this time, whilst maintaining the reaction flask at -78°C , NaBH_4 (7.5 g, 198.26 mmol) was added carefully in portions via spatula over 2-3 min. The reaction mixture was thereafter allowed to warm to 0°C whereupon a second batch of NaBH_4 (7.5 g, 198.26 mmol) was added in one portion. After 10 min at 0°C , TLC analysis revealed that a slower-moving major product had formed and that no starting alkene **18** remained. The reaction mixture was carefully quenched by the cautious dropwise addition of 3N aqueous AcOH until pH 7 was attained. The solvents were removed *in vacuo*. The residue was taken up in EtOAc (500 mL), washed with H_2O (100 mL) and brine (100 mL), dried (MgSO_4), filtered and concentrated *in vacuo*. The residue was purified by SiO_2 flash chromatography with petrol:EtOAc (gradient elution 5:1 to 2:1) to give the title alcohol **19** (10.3 g, 78%).

Data for **19**: $[\alpha]_D +6.48^\circ$ (c 0.648, CH_2Cl_2); IR 3429 (br), 2936 (m), 1719 (s), 1450 (w), 1275 (s), 1167 (w), 1103 (s), 1167 (w), 1030 (w), 932 (w), 714 (m) cm^{-1} ; ^1H NMR (500 MHz, CDCl_3 , 298K) δ 8.02-7.90 (m, 2H, Ph), 7.57-7.47 (m, 1H, Ph), 7.45-7.33 (m, 2H, Ph), 4.30 (dd, 1H, $J = 4.7, 11.4$ Hz, H-6a), 4.20 (dd, 1H, $J = 6.4, 11.4$ Hz, H-6b), 4.08 (m, 2H, H-9a, H-8), 3.77 (m, 1H, H-12a), 3.72 (m, 1H, H-12b), 3.69 (m, 1H, H-9b), 2.89 (br s, 1H, OH-12), 2.09 (m, 1H, H-7), 1.86 (m, 1H, H-11a), 1.74 (m, 1H, H-11b), 1.63-1.46 (m, 8 H, cyclohex), 1.40-1.28 (m, 2H, cyclohex) ppm; ^{13}C NMR (125 MHz, CDCl_3 , 298K) δ 166.29 (C=O), 133.04 (Ph), 129.69 (Ph q), 129.40 (Ph), 128.35 (Ph), 109.30 (-O-C-O-), 76.93 (C-8), 67.97 (C-9), 65.41 (C-6),

60.77 (C-12), 39.45 (C-7), 36.03 (cyclohex), 34.98 (cyclohex), 32.16 (C-11), 24.93 (cyclohex), 23.81 (cyclohex), 23.74 (cyclohex) ppm; VG 70-SE Positive Ion FAB HRMS: Calcd. for $C_{19}H_{26}NaO_5$ ($M+Na$)⁺: 357.16778. Found: 357.16823.

Silyl Ether **20** (II-YL-122)

To a stirred rt solution of alcohol **19** (25.4 g, 75.96 mmol) in dry DMF (200 mL) under N_2 was added t -BuPh₂SiCl (21.76 mL, 83.7 mmol) followed by imidazole (6.72 g, 98.7 mmol). The reactants were stirred at rt for 4 h whereupon TLC analysis indicated that no starting alcohol **19** remained. MeOH (2 mL) was added and the solvents were removed *in vacuo*. The oily residue was dissolved in Et₂O (500 mL), successively washed with H₂O (50 mL) and brine (50 mL), and then dried over MgSO₄. After filtration and concentration *in vacuo*, the residue was purified by SiO₂ flash chromatography using petrol:Et₂O (gradient elution 20:1 to 10:1) to give **20** (39.7 g, 91%) as a colorless oil.

Data for **20**: [α]_D +7.2 ° (*c* 0.708, CH₂Cl₂); IR 2936 (m), 2858 (w), 1720 (s), 1429 (w), 1366 (w), 1273 (s), 1165 (w), 1105 (s), 1032 (w), 932 (w), 824 (w), 739 (w), 706 (s), 613 (w) cm⁻¹; ¹H NMR (500 MHz, CDCl₃, 298K) δ 8.08-8.02 (m, 2H, Ph), 7.77-7.67 (m, 4H, Ph), 7.56 (m, 1H, Ph), 7.48-7.34 (m, 8H, Ph), 4.39 (dd, 1H, J = 4.7, 11.3 Hz, H-6a), 4.32 (dd, 1H, J = 6.4, 11.4 Hz, H-6b), 4.19 (m, 1H, H-8), 4.11 (dd, 1H, J = 6.2, 8.1 Hz, H-9a), 3.88 (m, 2H, H-12a, H-12b), 3.78 (dd, 1H, J = 7.5, 7.8 Hz, H-9b), 2.25 (m, 1H, H-7), 2.04 (m, 1H, H-11a), 1.74 (m, 1H, H-11b), 1.70-1.53 (m, 8 H, cyclohex), 1.46-1.35 (m, 2H, cyclohex), 1.10 (s, 9H, t -Bu) ppm; ¹³C NMR (125 MHz, CDCl₃, 298K) δ 166.22 (C=O), 135.45 (Ph), 135.44 (Ph), 133.64 (Ph), 133.62 (Ph), 132.87 (Ph), 130.01 (Ph), 129.54 (Ph), 129.44 (Ph), 128.30 (Ph), 127.57 (Ph), 127.56 (Ph), 109.07 (-O-C-O-), 76.56 (C-8), 67.62 (C-9), 65.11 (C-6), 61.88 (C-12), 38.26 (C-7), 36.16 (cyclohex), 34.94 (cyclohex), 30.92 (C-11), 26.79 (-C(Me)₃), 25.11 (cyclohex), 23.88 (cyclohex), 23.77 (cyclohex), 19.08 (-C(Me)₃) ppm; VG 70-SE Positive Ion FAB HRMS: Calcd. for $C_{35}H_{44}NaO_5Si$ ($M+Na$)⁺: 595.28556. Found: 595.28414.

Alcohol **21** (II-YL-125)

To a rt solution of *O*-benzoate **20** (20.0 g, 34.9 mmol) in MeOH (50 mL) was added K₂CO₃ (0.24 g, 1.74 mmol). The reaction mixture was stirred for 72 h, whereafter it was concentrated *in vacuo*. The residue was taken up in Et₂O (500 mL), washed successively with H₂O (50 mL), brine (50 mL), and dried over MgSO₄. After filtration, concentration *in vacuo* furnished a residue that was purified by SiO₂ flash chromatography with petrol:Et₂O (gradient elution 6:1 to 2:1). Alcohol **21** (15.6 g, 95%) was isolated as a colorless oil.

Data for **21**: [α]_D +1.57 ° (*c* 0.382, CH₂Cl₂); IR 3456 (br w), 2936 (s), 2860 (m), 1429 (w), 1363 (w), 1279 (w), 1161 (w), 1107 (s), 1038 (m), 934 (w), 824 (w), 739 (w), 702 (s), 613 (w), 502 (m) cm⁻¹; ¹H NMR (500 MHz, CDCl₃, 298K) δ 7.70-7.64 (m, 4H, Ph), 7.45-7.36 (m, 6H, Ph), 4.19 (dd, 1H, *J* = 6.3, 12.7 Hz, H-8), 4.01 (dd, 1H, *J* = 6.3, 8.2 Hz, H-9a), 3.80 (m, 1H, H-12a), 3.74 (m, 1H, H-12b), 3.70 (dd, 1H, *J* = 7.8, 7.9 Hz, H-9b), 3.67 (dd, 1H, *J* = 5.7, 11.3 Hz, H-6a), 3.60 (dd, 1H, *J* = 4.6, 11.3 Hz, H-6b), 3.01 (br s, 1H, OH), 1.96 (m, 1H, H-7), 1.76 (m, 1H, H-11a), 1.64 (m, 1H, H-11b), 1.64-1.47 (m, 8 H, cyclohex), 1.43-1.33 (m, 2H, cyclohex), 1.07 (s, 9H, *t*-Bu) ppm; ¹³C NMR (125 MHz, CDCl₃, 298K) δ 135.45 (Ph), 133.23 (Ph), 133.21 (Ph), 129.68 (Ph), 127.65 (Ph), 109.09 (-O-C-O-), 77.11 (C-8), 66.76 (C-9), 63.37 (C-6), 62.43 (C-12), 41.10 (C-7), 36.09 (cyclohex), 34.70 (cyclohex), 30.39 (C-11), 26.74 (-C(Me)₃), 25.07 (cyclohex), 23.91 (cyclohex), 23.73 (cyclohex), 19.02 (-C(Me)₃) ppm; VG 70-SE Positive Ion FAB HRMS: Calcd. for C₂₈H₄₀NaO₄Si (M+Na)⁺: 491.25934. Found: 491.25812.

Aldehyde **23** (II-YL-166)

To a rt solution of alcohol **21** (13.2 g, 28.2 mmol) in dry CH₂Cl₂ (200 mL) under N₂ was added [bis(acetoxy)iodo]benzene **22** (37.2 g, 0.116 mol, 4.1 equiv) in one portion followed by TEMPO (0.72 g, 4.61 mmol, 0.16 equiv), also in one portion. Stirring was continued for 1.5 h whereafter TLC analysis revealed that all of the starting alcohol **21** had been consumed and that a single faster-moving major product had formed. The reaction mixture was concentrated *in vacuo*, Et₂O (50 mL) was added, precipitated solids were filtered off, and the filtrate was concentrated *in vacuo*. The residue was purified by SiO₂ flash chromatography using petrol:Et₂O as eluent (3:1). Aldehyde **23** (12.5 g, 95%) was obtained as a colorless oil.

Data for **23**: [α]_D +9.86 ° (*c* 0.284, CH₂Cl₂); IR 2936 (s), 2858 (m), 1722 (m), 1429 (w), 1364 (w), 1163 (w), 1107 (s), 1038 (w), 932 (w), 824 (w), 739 (wm), 704 (s), 613 (w) cm⁻¹; ¹H NMR (500 MHz, C₆D₆, 298K) δ 9.52 (s, 1H, H-6), 7.76-7.64 (m, 4H, Ph), 7.30-7.16 (m, 6H, Ph), 4.14 (dd, 1H, *J* = 6.5, 13.1 Hz, H-8), 3.99 (dd, 1H, *J* = 6.4, 8.2 Hz, H-9a), 3.69 (m, 1H, H-12a), 3.60 (m, 1H, H-12b), 3.52 (dd, 1H, *J* = 6.9, 7.9 Hz, H-

9b), 2.32 (m, 1H, H-7), 1.91 (m, 1H, H-11a), 1.77 (m, 1H, H-11b), 1.65-1.42 (m, 8 H, cyclohex), 1.30-1.15 (m, 2H, cyclohex), 1.12 (s, 9H, *t*-Bu) ppm; ^{13}C NMR (125 MHz, C_6D_6 , 298K) δ 201.74 (C-6), 135.90 (Ph), 133.76 (Ph q), 133.70 (Ph q), 130.05 (Ph), 130.03 (Ph), 109.27 (-O-C-O-), 74.17 (C-8), 67.98 (C-9), 62.00 (C-12), 53.20 (C-7), 36.65 (cyclohex), 35.07 (cyclohex), 29.12 (C-11), 26.97 (-C(Me)₃), 25.49 (cyclohex), 24.28 (cyclohex), 24.10 (cyclohex), 19.26 (-C(Me)₃) ppm; VG 70-SE Positive Ion FAB HRMS: Calcd. for $\text{C}_{28}\text{H}_{38}\text{NaO}_4\text{Si}$ ($\text{M}+\text{Na}$)⁺: 489.24369. Found: 489.24277.

Enoate **24** (II-YL-167)

To a stirred solution of aldehyde **23** (12.5 g, 26.8 mmol) in dry CH_2Cl_2 (200 mL) under N_2 was added (carbomethoxymethylene)triphenylphosphorane (22.4 g, 67.0 mmol, 2.5 equiv) in one portion. The reactants were stirred at rt for 12 h before Et_2O (250 mL) was added. After removal of the precipitated $\text{Ph}_3\text{P}=\text{O}$ by filtration, the solvents were removed *in vacuo*, and the residue was purified by SiO_2 flash chromatography using petrol: Et_2O (7:1) as eluent. Enoate **24** (13.2 g, 94%) was obtained as a colorless oil.

Data for **24**: $[\alpha]_{\text{D}} +7.65^\circ$ (*c* 0.614, CH_2Cl_2); IR 2936 (s), 2858 (m), 1726 (s), 1655 (w), 1431 (w), 1273 (m), 1217 (w), 1165 (m), 1107 (s), 1038 (m), 932 (w), 824 (w), 739 (w), 704 (s) cm^{-1} ; ^1H NMR (500 MHz, C_6D_6 , 298K) δ 7.78-7.68 (m, 4H, Ph), 7.30-7.18 (m, 6H, Ph), 6.75 (dd, 1H, $J = 9.5, 15.7$ Hz, H-6), 5.85 (dd, 1H, $J = 0.6, 15.7$ Hz, H-5), 3.71 (m, 1H, H-8), 3.63 (dd, 1H, $J = 6.2, 8.3$ Hz, H-9a), 3.59 (m, 1H, H-12a), 3.55 (m, 1H, H-12b), 3.43 (dd, 1H, $J = 6.5, 8.2$ Hz, H-9b), 3.40 (s, 3H, OMe), 2.49 (m, 1H, H-7), 2.06 (m, 1H, H-11a), 1.70-1.48 (m, 8 H, cyclohex), 1.34 (m, 1H, H-11b), 1.30-1.18 (m, 2H, cyclohex), 1.13 (s, 9H, *t*-Bu) ppm; ^{13}C NMR (125 MHz, C_6D_6 , 298K) δ 165.99 (C-4), 148.10 (C-6), 135.93 (Ph), 134.06 (Ph), 134.03 (Ph), 129.97 (Ph), 129.96 (Ph), 123.49 (C-5), 109.82 (-O-C-O-), 77.42 (C-8), 67.39 (C-9), 61.61 (C-12), 50.99 (OMe), 43.72 (C-7), 36.86 (cyclohex), 35.52 (cyclohex), 33.74 (C-11), 27.04 (-C(Me)₃), 25.55 (cyclohex), 24.32 (cyclohex), 24.17 (cyclohex), 19.36 (-C(Me)₃) ppm; VG 70-SE Positive Ion FAB HRMS: Calcd. for $\text{C}_{31}\text{H}_{42}\text{NaO}_5\text{Si}$ ($\text{M}+\text{Na}$)⁺: 545.26991. Found: 545.26894.

Allylic Alcohol **11** (II-YL-168)

To a stirred -78 °C solution of enoate **24** (13.5 g, 25.83 mmol) in dry CH₂Cl₂ (200 mL) under N₂ was added *i*-Bu₂AlH (1.5 M solution in PhMe, 42.8 mL, 64.2 mmol, 2.49 equiv) dropwise over 30 min. The mixture was stirred at -78 °C for 1.5 h whereafter TLC analysis revealed that a single slower-moving product had formed and no starting enoate **24** remained. Saturated aqueous Rochelle salt solution (30 mL) was cautiously added dropwise (NB effervescence occurs) followed by EtOAc (500 mL). The reaction mixture was warmed to rt and stirred for 40 min, before being transferred to a large separatory funnel. After partitioning had occurred, the organic layer was separated and the aqueous layer was further extracted with EtOAc (2 x 200 mL). The combined organic layers were washed with H₂O (200 mL), dried (MgSO₄), filtered and concentrated *in vacuo*. The residue was purified by SiO₂ flash chromatography with petrol:EtOAc (gradient elution 7:1 to 4:1) to give allylic alcohol **11** (11.0 g, 86%) as a colorless oil.

Data for **11**: [α]_D +5.32 ° (*c* 1.17, CH₂Cl₂); IR 3420 (br w), 2936 (s), 2860 (s), 1427 (w), 1364 (w), 1279 (w), 1163 (w), 1105 (s), 976 (w), 932 (w), 824 (w), 739 (w), 702 (s), 613 (w) cm⁻¹; ¹H NMR (500 MHz, CDCl₃, 298K) δ 7.70-7.63 (m, 4H, Ph), 7.44-7.33 (m, 6H, Ph), 5.61 (dt, 1H, *J* = 5.5, 15.5 Hz, H-5), 5.35 (ddt, 1H, *J* = 9.1, 15.5 Hz, H-6), 4.00 (d, 1H, *J* = 1.3 Hz, H-4a), 3.99 (d, 1H, *J* = 1.3 Hz, H-4b), 3.96-3.87 (m, 2H, H-8, H-9a), 3.71 (m, 1H, H-12a), 3.65 (m, 1H, H-12b), 3.64 (m, 1H, H-9b), 2.42 (m, 1H, H-7), 2.08 (m, 1H, H-11a), 1.74 (br s, 1H, OH), 1.68-1.49 (m, 8 H, cyclohex), 1.45 (m, 1H, H-11b), 1.42-1.32 (m, 2H, cyclohex), 1.05 (s, 9H, *t*-Bu) ppm; ¹³C NMR (125 MHz, CDCl₃, 298K) δ 135.50 (Ph), 133.85 (Ph q), 133.83 (Ph q), 131.94 (C-5), 130.87 (C-6), 129.47 (Ph), 127.504 (Ph), 127.50 (Ph), 109.55 (-O-C-O-), 77.96 (C-8), 67.34 (C-9), 63.10 (C-4), 61.35 (C-12), 43.18 (C-7), 36.36 (cyclohex), 35.03 (cyclohex), 33.87 (C-11), 26.76 (-C(Me)₃), 25.12 (cyclohex), 23.90 (cyclohex), 23.78 (cyclohex), 19.09 (-C(Me)₃) ppm; VG 70-SE Positive Ion FAB HRMS: Calcd. for C₃₀H₄₂NaO₄Si (M+Na)⁺: 517.27499. Found: 517.27390.

Epoxy Alcohol **25** (II-YL-134)

To a stirred suspension of 4Å molecular sieves (10 g) in dry CH₂Cl₂ (250 mL) under N₂ was added L-(+)-diisopropyl tartrate (0.637 mL, 3.03 mmol, 0.12 equiv) in one portion. The mixture was cooled to -20 °C and Ti(OPr-*i*)₄ (0.74 mL, 2.51 mmol, 0.1 equiv) was added in one portion. After 10 min, *t*-BuO₂H (8.69 M solution in CH₂Cl₂, 5.8 mL, 50.2 mmol, 2 equiv) was added dropwise over 5 min. The mixture was stirred at -20 °C for 30 min whereafter a solution of allylic alcohol **11** (12.5 g, 25.27 mmol) in dry CH₂Cl₂ (50 mL) was added dropwise over 30 min. The reactants were stirred at -20 °C for 12 h and then quenched with H₂O (50 mL). EtOAc (500 mL) was added and the reaction mixture was allowed to warm to rt. The organic layer was separated and washed with H₂O (200 mL), dried (MgSO₄), and filtered. Following evaporation of the solvent

in vacuo, the residue was purified by SiO₂ flash chromatography with petrol:EtOAc (4:1) as eluent to give **25** (10.3 g, 80%) as a colorless oil.

Data for **25**: [α]_D -6.95 ° (*c* 0.82, CH₂Cl₂); IR 3462 (br w), 2936 (s), 2859 (m), 1427 (w), 1364 (w), 1279 (w), 1107 (s), 1038 (w), 934 (w), 824 (w), 739 (w), 704 (s), 611 (w) cm⁻¹; ¹H NMR (500 MHz, CDCl₃, 298K) δ 7.68-7.63 (m, 4H, Ph), 7.43-7.34 (m, 6H, Ph), 4.09 (m, 1H, H-8), 3.95 (dd, 1H, *J* = 6.4, 8.2 Hz, H-9a), 3.83 (dd, 1H, *J* = 2.5, 12.6 Hz, H-4a), 3.79 (m, 2H, H-12a, H-12b), 3.64 (dd, 1H, *J* = 7.8, 8.0 Hz, H-9b), 3.54 (dd, 1H, *J* = 4.4, 12.6 Hz, H-4b), 2.96 (dt, 1H, *J* = 2.5, 4.6 Hz, H-5), 2.89 (dd, 1H, *J* = 2.3, 6.7 Hz, H-6), 1.90 (br s, 1H, OH), 1.80 (m, 1H, H-7), 1.77 (m, 1H, H-11a), 1.71 (m, 1H, H-11b), 1.62-1.47 (m, 8 H, cyclohex), 1.43-1.33 (m, 2H, cyclohex), 1.04 (s, 9H, *t*-Bu) ppm; ¹³C NMR (125 MHz, CDCl₃, 298K) δ 135.52 (Ph), 135.51 (Ph), 133.73 (Ph q), 133.71 (Ph q), 129.58 (Ph), 127.60 (Ph), 109.29 (-O-C-O-), 75.52 (C-8), 66.55 (C-9), 62.11 (C-12), 61.51 (C-4), 57.06 (C-5), 56.06 (C-6), 39.63 (C-7), 36.08 (cyclohex), 34.73 (cyclohex), 31.53 (C-11), 26.82 (-C(Me)₃), 25.10 (cyclohex), 23.91 (cyclohex), 23.76 (cyclohex), 19.13 (-C(Me)₃) ppm; VG 70-SE Positive Ion FAB HRMS: Calcd. for C₃₀H₄₂NaO₅Si (M+Na)⁺: 533.26991. Found: 533.27059.

Iodo Epoxide **10** (II-YL-136)

To a vigorously stirred rt solution of epoxy alcohol **25** (4.4 g, 8.62 mmol) in dry THF:MeCN (4:1, 100 mL) under N₂ was added imidazole (3.5 g, 51.41 mmol), Ph₃P (6.73 g, 25.66 mmol) and I₂ (6.52 g, 25.69 mmol) successively in single portions. Stirring was continued at rt for 0.5 h whereupon Et₂O (200 mL) was added to precipitate out Ph₃P=O. The solids were filtered through a short pad of SiO₂ gel, and the filter pad was washed with Et₂O until TLC analysis revealed that no more of **10** was emerging in the filtrate. The filtrate was concentrated *in vacuo* and the residue was purified by SiO₂ flash chromatography using petrol:Et₂O (7:1) as eluent. Iodide **10** (5.2 g, 97%) was obtained as colorless oil.

Data for **10**: [α]_D +0.95 ° (*c* 0.632, CH₂Cl₂); IR 2934 (s), 2858 (m), 1429 (w), 1364 (w), 1163 (w), 1105 (s), 1038 (w), 934 (w), 897 (w), 822 (w), 739 (w), 702 (s), 611 (w) cm⁻¹; ¹H NMR (500 MHz, C₆D₆, 298K) δ 7.82-7.75 (m, 4H, Ph), 7.24-7.20 (m, 6H, Ph), 3.85-3.80 (m, 4H, H-8, H-12a, H-12b, H-9a), 3.49 (m, 1H, H-9b), 2.63 (m, 1H, H-5), 2.62 (m, 1H, H-4a), 2.42 (m, 1H, H-4b), 2.33 (dd, 1H, *J* = 1.6, 7.2 Hz, H-6), 1.94 (m, 1H, H-11a), 1.72 (m, 1H, H-11b), 1.67-1.54 (m, 8 H, cyclohex), 1.53 (m, 1H, H-7), 1.32-1.22 (m, 2H, cyclohex), 1.16 (s, 9H, *t*-Bu) ppm; ¹³C NMR (125 MHz, C₆D₆, 298K) δ 136.01 (Ph), 135.98 (Ph), 134.25 (Ph q), 134.22 (Ph q), 129.95 (Ph), 109.36 (-O-C-O-), 75.77 (C-8), 67.76 (C-9), 62.79 (C-6), 62.46 (C-12), 56.78 (C-5), 40.74 (C-7), 36.70 (cyclohex), 35.43 (cyclohex), 32.11 (C-11), 27.11 (-C(Me)₃), 25.56 (cyclohex), 24.35 (cyclohex), 24.21 (cyclohex), 19.43 (-C(Me)₃), 4.82 (C-4) ppm; VG 70-SE Positive Ion FAB HRMS: Calcd. for C₃₀H₄₁INaO₄Si (M+Na)⁺: 643.17164. Found: 643.17024.

Allylic Alcohol **26** (II-YL-137)

To a vigorously stirred solution of iodide **10** (5.0 g, 8.06 mmol) in MeOH (100 mL) was added Zn dust (5.2 g, 79.52 mmol) and the reaction mixture was heated at reflux for 4 h. After cooling to rt, it was filtered through a short pad of SiO₂, which was washed well with MeOH. Concentration of the filtrate *in vacuo* and purification of the residue by SiO₂ flash chromatography with petrol:EtOAc (7:1) as eluent furnished allylic alcohol **26** (3.61 g, 91%) as a colorless oil.

Data for **26**: $[\alpha]_D^{25} +17.3^\circ$ (*c* 0.902, CH₂Cl₂); IR 3452 (br w), 2936 (s), 2858 (m), 1429 (w), 1364 (w), 1281 (w), 1161 (w), 1107 (s), 1038 (m), 999 (m), 932 (m), 824 (w), 739 (w), 704 (s), 613 (w) cm⁻¹; ¹H NMR (500 MHz, CDCl₃, 298K) δ 7.70-7.64 (m, 4H, Ph), 7.45-7.34 (m, 6H, Ph), 5.83 (ddd, 1H, *J* = 5.2, 10.5, 17.1 Hz, H-5), 5.28 (ddd, *J* = 1.6, 1.6, 17.2 Hz, H-4b), 5.14 (ddd, 1H, *J* = 1.6, 1.6, 10.5 Hz, H-4a), 4.28 (m, 1H, H-8), 4.25 (m, 1H, H-6), 4.03 (dd, 1H, *J* = 6.3, 8.2 Hz, H-9a), 3.77 (m, 1H, H-12a), 3.73 (dd, 1H, *J* = 7.7, 7.9 Hz, H-9b), 3.69 (m, 1H, H-12b), 3.16 (br s, 1H, OH), 1.86 (m, 1H, H-7), 1.82-1.76 (m, 2H, H-11a, H-11b), 1.63-1.45 (m, 8 H, cyclohex), 1.43-1.30 (m, 2H, cyclohex), 1.07 (s, 9H, *t*-Bu) ppm; ¹³C NMR (125 MHz, CDCl₃, 298K) δ 139.34 (C-5), 135.51 (Ph), 133.31 (Ph q), 129.64 (Ph), 129.62 (Ph), 127.62 (Ph), 115.03 (C-4), 109.04 (-O-C-O-), 76.70 (C-8), 73.66 (C-6), 67.45 (C-9), 62.79 (C-12), 43.25 (C-7), 36.13 (cyclohex), 34.73 (cyclohex), 27.68 (C-11), 26.78 (-C(Me)₃), 25.11 (cyclohex), 23.93 (cyclohex), 23.79 (cyclohex), 19.06 (-C(Me)₃) ppm; VG 70-SE Positive Ion FAB HRMS: Calcd. for C₃₀H₄₂NaO₄Si (M+Na)⁺: 517.27499. Found: 517.27438.

Diol **9** (II-YL-138)

To a stirred solution of *O*-silyl ether **26** (8.7 g, 17.59 mmol) in dry THF (150 mL) under N₂ at 0 °C was added tetra-*n*-butylammonium fluoride (1 M solution in THF, 20.9 mL, 20.9 mmol, 1.19 equiv) in one portion. The cooling bath was removed and the reaction mixture was allowed to stir at rt for 1 h, whereafter it was concentrated *in vacuo*. The residue was purified by SiO₂ flash chromatography with petrol:EtOAc (1:2) as eluent; diol **9** (4.1 g, 91%) was obtained as a colorless oil.

Data for **9**: $[\alpha]_D^{+25.5}$ (c 0.318, CH_2Cl_2); IR 3389 (br m), 2935 (s), 2860 (m), 1645 (w), 1447 (w), 1366 (w), 1279 (w), 1232 (m), 1103 (s), 1038 (m), 995 (m), 930 (s) cm^{-1} ; ^1H NMR (500 MHz, CDCl_3 , 298K) δ 5.81 (ddd, 1H, J = 5.3, 10.5, 17.2 Hz, H-5), 5.23 (ddd, J = 1.6, 1.6, 17.2 Hz, H-4b), 5.14 (ddd, 1H, J = 1.5, 1.6, 10.6 Hz, H-4a), 4.17 (m, 1H, H-8), 4.11 (m, 1H, H-6), 4.07 (dd, 1H, J = 6.0, 8.1 Hz, H-9a), 3.66 (br m, 2H, H-12a, and H-12b), superimposed upon 3.65 (dd, 1H, J = 8.0, 8.0 Hz, H-9b), 3.45 (br t, 1H, OH-12), 3.41 (br d, 1H, J = 4.5 Hz, OH-6), 1.80-1.67 (m, 3H, H-11a, H-11b, H-7), 1.62-1.42 (m, 8 H, cyclohex), 1.41-1.26 (m, 2H, cyclohex) ppm; ^{13}C NMR (125 MHz, CDCl_3 , 298K) δ 139.08 (C-5), 115.46 (C-4), 109.11 (-O-C-O-), 76.43 (C-8), 73.47 (C-6), 67.91 (C-9), 61.04 (C-12), 45.14 (C-7), 36.17 (cyclohex), 34.89 (cyclohex), 29.13 (C-11), 25.02 (cyclohex), 23.91 (cyclohex), 23.80 (cyclohex) ppm; VG 70-SE Positive Ion FAB HRMS: Calcd. for $\text{C}_{14}\text{H}_{24}\text{NaO}_4$ ($\text{M}+\text{Na}$) $^+$: 279.15722. Found: 279.15731.

γ -Butyrolactone **7** (II-YL-140)

To a stirred rt solution of diol **9** (1.07 g, 4.17 mmol) in dry CH_2Cl_2 (40 mL) under N_2 was sequentially added [bis(acetoxy)iodo]benzene **22** (6.73 g, 20.89 mmol, 5 equiv) and TEMPO (131 mg, 0.838 mmol, 0.2 equiv) in single portions. The reactants were stirred at rt for 5 h whereafter TLC analysis indicated that a single faster-moving product had formed. Saturated aqueous sodium thiosulfate (50 mL) and Et_2O (100 mL) were added, and the organic layer was separated and washed successively with saturated aqueous NaHCO_3 (10 mL) and H_2O (10 mL) before being dried (MgSO_4), filtered, and concentrated *in vacuo*. Purification of the residue by SiO_2 flash chromatography gave the lactone **7** (0.99 g, 94%) as a colorless oil.

Data for **7**: $[\alpha]_D^{+48.6}$ (c 0.42, CH_2Cl_2); IR 2937 (s), 2860 (w), 1782 (s), 1425 (w), 1366 (w), 1273 (w), 1169 (m), 1105 (s), 991 (w), 934 (m), 853 (w) cm^{-1} ; ^1H NMR (500 MHz, CDCl_3 , 298K) δ 5.80 (ddd, 1H, J = 6.8, 10.4, 17.2 Hz, H-5), 5.35 (ddd, J = 1.1, 1.1, 17.1 Hz, H-4b), 5.25 (ddd, 1H, J = 1.0, 1.0, 10.4 Hz, H-4a), 4.70 (dd, 1H, J = 7.0, 7.0 Hz, H-6), 4.12 (ddd, 1H, J = 4.3, 6.6, 10.8 Hz, H-8), 4.01 (dd, 1H, J = 6.5, 8.3 Hz, H-9a), 3.50 (dd, 1H, J = 6.7, 8.3 Hz, H-9b), 2.61 (dd, 1H, J = 8.6, 17.5 Hz, H-11a), 2.50 (1H, J = 8.7, 17.5 Hz, H-11b), 2.35 (m, 1H, H-7), 1.62-1.42 (m, 8 H, cyclohex), 1.41-1.28 (m, 2H, cyclohex) ppm; ^{13}C NMR (125 MHz, CDCl_3 , 298K) δ 175.59 (C-12), 134.55 (C-5), 118.68 (C-4), 110.08 (-O-C-O-), 82.29 (C-6), 73.44 (C-8), 67.02 (C-9), 44.20 (C-7), 35.80 (cyclohex), 34.45 (cyclohex), 29.22 (C-11), 24.94 (cyclohex), 23.77 (cyclohex), 23.59 (cyclohex) ppm; VG 70-SE Positive Ion FAB HRMS: Calcd. for $\text{C}_{14}\text{H}_{20}\text{NaO}_4$ ($\text{M}+\text{Na}$) $^+$: 275.12592. Found: 275.12622.

γ -Butyrolactone O-Pivaloate **41** (II-YL-174)

Part 1. Preparation and Partial Purification of Diol **27** (II-YL-182)

To a stirred $-40\text{ }^{\circ}\text{C}$ solution of cyclohexylidene acetal **7** (0.3 g, 1.19 mmol) in dry CH_2Cl_2 (6 mL) under N_2 was added 1,3-propanedithiol (1.2 mL, 11.95 mmol, 10 equiv) in one portion followed by boron trifluoride etherate (0.17 mL, 1.34 mmol, 1.13 equiv). After 2 min at $-40\text{ }^{\circ}\text{C}$, TLC analysis of the reaction mixture indicated that no starting acetal **7** remained, and that a slower-moving major product had formed. The reaction was quenched by adding Et_3N (2 mL). The reaction mixture was then applied directly to the top of a SiO_2 flash chromatography column which was eluted initially with CH_2Cl_2 to remove the excess thiol and 1,3-dithiane by-product. Further elution with 10:1 CH_2Cl_2 :MeOH eventually provided the desired diol **27** (0.205 g) as a slightly yellow oil after concentration *in vacuo*. It was used directly for the next step without further chromatographic purification *to minimise the risk of lactone migration to the C(8)-hydroxyl*. In this regard, we recommend that the C(8) and C(9)-hydroxyls of **27** be immediately protected and that the compound be used directly for the next reaction without being stored at this stage.

Data for **27**: $[\alpha]_{\text{D}}^{25} +55.25^{\circ}$ (c 0.724, MeOH); IR 3385 (br s), 2932 (w), 1767 (s), 1639 (w), 1556 (w), 1421 (w), 1271 (w), 1204 (s), 1080 (m), 991 (m), 945 (m), 887 (w) cm^{-1} ; ^1H NMR (500 MHz, CDCl_3 , 298K) δ 5.83 (ddd, 1H, $J = 7.0, 10.4, 17.2\text{ Hz}$, H-5), 5.39 (ddd, $J = 1.0, 1.0, 17.1\text{ Hz}$, H-4b), 5.30 (ddd, 1H, $J = 1.0, 1.0, 10.4\text{ Hz}$, H-4a), 4.82 (br m, 1H, H-6), 3.79 (ddd, 1H, $J = 3.5, 3.8, 7.3\text{ Hz}$, H-8), 3.62 (dd, 1H, $J = 3.5, 11.0\text{ Hz}$, H-9a), 3.46 (dd, 1H, $J = 7.7, 11.0\text{ Hz}$, H-9b), 2.73 (dd, 1H, $J = 9.3, 17.6\text{ Hz}$, H-11a) superimposed upon 2.73 (br s, 2H, OH), 2.47 (dd, 1H, $J = 8.9, 17.6\text{ Hz}$, H-11b), 2.31 (m, 1H, H-7), ppm; ^{13}C NMR (125 MHz, CDCl_3 , 298K) δ 176.79 (C-12), 134.65 (C-5), 119.17 (C-4), 82.74 (C-6), 69.37 (C-8), 65.28 (C-9), 43.95 (C-7), 28.88 (C-11) ppm; CI HRMS: Calcd. for $\text{C}_8\text{H}_{13}\text{O}_4$ ($\text{M}+\text{H}$) $^{+}$: 173.08138. Found: 173.08184.

Part 2. Preparation of O-Pivaloate **41** (II-YL-174)

To diol **27** (0.205 g, *ca* 1.19 mmol) in dry pyridine (3 mL) at $0\text{ }^{\circ}\text{C}$ was added pivaloyl chloride (0.3 mL, 2.44 mmol, 2.05 equiv) over 2 min. The reactants were stirred under N_2 at $0\text{ }^{\circ}\text{C}$ for 1 h and then allowed to warm to rt, where they were kept for 12 h. MeOH (1 mL) was added, and the reaction mixture was diluted with EtOAc (25 mL), filtered through a short pad of SiO_2 and the filtrate evaporated *in vacuo*. The residue was purified by SiO_2 flash chromatography with petrol:EtOAc (2:1) as eluent to give O-pivaloate **41** (0.24 g, 79%) as slightly yellow oil.

(Again, due to the potential for lactone migration involving the C(8)-OH, we recommend that **41** be used directly for the next step.)

Data for **41**: $[\alpha]_D^{+36.14}$ ° (*c* 0.498, CH₂Cl₂); IR 3468 (br m), 2972 (m), 2937 (w), 2878 (w), 1773 (s), 1728 (s), 1404 (w), 1285 (s), 1163 (s), 991 (m), 943 (m) cm⁻¹; ¹H NMR (500 MHz, CDCl₃, 298K) δ 5.79 (ddd, 1H, *J* = 7.1, 10.4, 17.3 Hz, H-5), 5.36 (d of narrow t, *J* = 17.1 Hz, H-4b), 5.27 (d, 1H, *J* = 10.4 Hz, H-4a), 4.79 (dd, 1H, *J* = 7.2, 8.0 Hz, H-6), 4.04 (dd, 1H, *J* = 4.4, 11.5 Hz, H-9a), 3.95 (dd, 1H, *J* = 6.5, 11.5 Hz, H-9b), 3.89 (br m, 1H, H-8), 3.13 (br d, *J* = 4.2 Hz, C-8-OH), 2.74 (dd, 1H, *J* = 9.7, 17.5 Hz, H-11a), 2.45 (dd, 1H, *J* = 8.8, 17.5 Hz, H-11b), 2.31 (br ddd, 1H, *J* = 3.1, 8.8, 17.8 Hz, H-7), 1.16 (s, 9H, OC(O)CMe₃) ppm; ¹³C NMR (125 MHz, CDCl₃, 298K) δ 178.69 (C=O of Piv), 176.27 (C-12), 134.47 (C-5), 119.28 (C-4), 82.33 (C-6), 66.87 (C-9), 66.73 (C-8), 44.30 (C-7), 38.74 (OC(O)CMe₃), 28.53 (C-11), 27.03 (OC(O)CMe₃) ppm; VG 70-SE Positive Ion FAB HRMS: Calcd. for C₁₃H₂₀NaO₅ (M+Na)⁺: 279.12084. Found: 279.12075.

O-Silylated Butyrolactone **28** (II-YL-176)

To a stirred 0 °C solution of **41** (0.59 g, 2.30 mmol) in dry CH₂Cl₂ (10 mL) under N₂ was successively added 2,6-lutidine (0.80 mL, 6.87 mmol, 2.98 equiv) and Et₃SiOTf (0.62 mL, 2.74 mmol, 1.19 equiv) in single portions. Stirring was continued at 0 °C for 1 h whereafter TLC analysis revealed that all of the starting alcohol **41** had been consumed. Excess solid NaHCO₃ was added followed by Et₂O (80 mL) and saturated aqueous sodium bicarbonate (20 mL). The organic layer was separated and washed successively with H₂O (20 mL) and brine (20 mL), before being dried over MgSO₄, filtered, and concentrated *in vacuo*. Purification of the crude residue by SiO₂ flash chromatography with petrol:EtOAc (8:1) furnished the O-silyl ether **28** (0.79 g, 93%) as a colorless oil. 500 MHz ¹H NMR analysis of **28** typically revealed that it was typically a 15:1-20:1 mixture of **28** (as the major component) and a molecule we have tentatively assigned as the C(8)-O-lactonised product **42**.

Data for **28**: $[\alpha]_D^{+49.3}$ ° (*c* 0.430, CH₂Cl₂); IR 2959 (s), 2912 (w), 2880 (m), 1786 (s), 1732 (s), 1460 (w), 1418 (w), 1369 (w), 1283 (w), 1238 (w), 1151 (s), 1080 (m), 1005 (s), 935 (w), 739 (s) cm⁻¹; ¹H NMR (500 MHz, CDCl₃, 298K) δ 5.80 (ddd, 1H, *J* = 6.9, 10.4, 17.2 Hz, H-5), 5.35 (dt, *J* = 1.0, 17.1 Hz, H-4b), 5.28 (dt, 1H, *J* = 1.0, 10.4 Hz, H-4a), 4.66 (m, 1H, H-6), 4.03 (dd, 1H, *J* = 4.1, 11.0 Hz, H-9a), 3.91 (ddd, 1H, *J* = 2.2, 4.1, 6.4 Hz, H-8), 3.84 (dd, 1H, *J* = 6.9, 11.0 Hz, H-9b), 2.77 (dd, 1H, *J* = 9.2, 17.2 Hz, H-11a), 2.44 (dd, 1H, *J* = 8.8, 17.2 Hz, H-11b), 2.37 (m, 1H, H-7), 1.16 (s, 9H, OC(O)CMe₃), 0.93 (t, 9H, *J* = 8.0 Hz, Me of TES), 0.61 (2 x q superimposed upon one another, 6H, -CH₂- of TES) ppm; ¹³C NMR (125 MHz, CDCl₃, 298K) δ 178.00 (C=O of Piv), 175.98 (C-12), 134.83 (C-5), 118.87 (C-4), 82.00 (C-6), 67.12 (C-8), 66.02 (C-9), 45.04 (C-7), 38.69 (OC(O)CMe₃), 28.14 (C-11), 27.10 (OC(O)CMe₃), 6.70 (MeCH₂- of TES), 4.91 (MeCH₂- of TES) ppm; VG 70-SE Positive Ion FAB HRMS: Calcd. for C₁₉H₃₄NaO₅Si (M+Na)⁺: 393.20731. Found: 393.20688.

β -Ketoester 29 (II-YL-155)

To a -78°C solution of lactone **28** (1.12 g, 3.02 mmol) in dry THF (20 mL) under N_2 was added $\text{LiN}(\text{SiMe}_3)_2$ (1 M solution in THF, 6.7 mL, 6.7 mmol, 2.01 equiv) dropwise over 5 min. Stirring was continued for a further 30 min before a solution of isobutyryl imidazole **8** (1.25 g, 9.05 mmol, 3 equiv) in dry THF (1 mL) was added dropwise over 5 min. After stirring at -78°C for 1.5 h, the reaction was quenched at -78°C with saturated aqueous NH_4Cl (20 mL), and diluted with Et_2O (100 mL). The organic layer was separated and washed successively with H_2O (2 x 20 mL) and brine (20 mL), dried over MgSO_4 and filtered. The filtrate was concentrated *in vacuo* and the residue was purified by SiO_2 flash chromatography with petrol:EtOAc (20:1) to give **29** (0.89 g, 67%).

Data for **29**: $[\alpha]_D^{+21.8}$ (c 0.924, CH_2Cl_2); IR 2964 (s), 2882 (m), 1774 (s), 1728 (s), 1468 (w), 1375 (w), 1283 (m), 1150 (s), 1005 (s), 941 (m), 739 (s) cm^{-1} ; ^1H NMR (500 MHz, C_6D_6 , 298 K) δ 5.67 (ddd, 1H, J = 7.3, 10.3, 17.4 Hz, H-5), 5.17 (br d, J = 17.1 Hz, H-4b), 4.93 (d, 1H, J = 10.3 Hz, H-4a), 4.60 (dd, 1H, J = 7.5, 7.6 Hz, H-6), 4.24 (dd, 1H, J = 8.4 Hz, H-11), 4.02 (dd, 1H, J = 5.3, 11.1 Hz, H-9a), 3.93 (m, 1H, H-8), 3.69 (dd, 1H, J = 8.2, 11.1 Hz, H-9b), 3.25 (ddd, 1H, J = 1.9, 8.1, 8.1 Hz, H-7), 3.21 (septet, 1H, J = 6.9 Hz, H-17), 1.18 (s, 9H, $\text{OC}(\text{O})\text{CMe}_3$), 1.09 (d, 3H, J = 6.6 Hz, Me-18 or Me-19), 1.01 (d, 3H, J = 7.2 Hz, Me-18 or Me-19), 0.86 (t, 9H, J = 8.0 Hz, Me of TES), 0.52-0.44 (2 x q superimposed upon one another, 6H, J = 7.8, 7.9 Hz, $-\text{CH}_2-$ of TES) ppm; ^{13}C NMR (125 MHz, C_6D_6 , 298 K) δ 206.14 ($\text{C}-16$), 177.33 ($\text{C}=\text{O}$ of Piv), 171.21 ($\text{C}-12$), 135.53 ($\text{C}-5$), 118.88 ($\text{C}-4$), 81.08 ($\text{C}-6$), 67.90 ($\text{C}-8$), 65.32 ($\text{C}-9$), 50.86 ($\text{C}-11$), 45.85 ($\text{C}-7$), 40.68 ($\text{C}-17$), 38.77 ($\text{OC}(\text{O})\text{CMe}_3$), 27.21 ($\text{OC}(\text{O})\text{CMe}_3$), 18.73 (Me-18 or Me-19), 17.34 (Me-18 or Me-19), 6.89 (MeCH_2- of TES), 5.17 (MeCH_2- of TES) ppm; VG 70-SE Positive Ion FAB HRMS: Calcd. for $\text{C}_{23}\text{H}_{40}\text{NaO}_6\text{Si}$ ($\text{M}+\text{Na}$) $^+$: 463.24917. Found: 463.24980.

β -Ketoester 30 (II-YL-159)

To a stirred 0°C solution of **29** (0.34 g, 0.772 mmol) in dry DMF (6 mL) under N_2 was added NaH (60% dispersion in mineral oil, 35.3 mg, 0.883 mmol, 1.14 equiv) in one portion. The mixture was stirred at 0°C for

30 min and MeI (1 mL, 16.06 mmol, 20.8 equiv) was added in one portion. Stirring was continued at 0 °C for 2 h, whereafter TLC analysis indicated that a single slightly-slower-moving major product had formed. Saturated aqueous NH₄Cl (10 mL) was added to the reaction mixture followed by Et₂O (50 mL) and the organic layer was separated. The aqueous layer was further extracted with Et₂O (10 mL) and the combined organic layers were washed with H₂O (10 mL), dried over MgSO₄, filtered, and concentrated *in vacuo*. Purification of the residue by SiO₂ flash chromatography with petrol:Et₂O (10:1) gave **30** (0.31 g, 89%) as a colorless oil.

Data for **30**: [α]_D +29.5 ° (*c* 0.234, CH₂Cl₂); IR 2963 (s), 2912 (m), 2880 (m), 1773 (s), 1732 (s), 1703 (m), 1462 (m), 1377 (w), 1323 (w), 1283 (m), 1244 (m), 1204 (m), 1157 (s), 1128 (s), 1009 (s), 945 (m), 739 (s) cm⁻¹; ¹H NMR (500 MHz, C₆D₆, 298 K) δ 5.50 (ddd, 1H, *J* = 8.0, 10.2, 18.2 Hz, H-5), 5.13 (dt, 1H, *J* = 17.1 Hz, H-4b), 4.96 (br dt, 1H, *J* = 10.3 Hz, H-4a), 4.85 (dd, 1H, *J* = 8.0, 10.0 Hz, H-6), 4.31 (m, 1H, H-8), 4.13 (dd, 1H, *J* = 4.5, 12.4 Hz, H-9a), 3.97 (dd, *J* = 3.5, 12.4 Hz, H-9b), 2.94 (septet, 1H, *J* = 6.7, Hz, H-17), 2.35 (dd, 1H, *J* = 7.3, 10.0 Hz, H-7), 1.65 (s, 3H, Me-13), 1.10 (s, 9H, OC(O)CMe₃), 1.07 (d, 3H, *J* = 6.7 Hz, Me-18 or Me-19), 1.04 (d, 3H, *J* = 6.6 Hz, Me-18 or Me-19), 0.89 (t, 9H, *J* = 8.0 Hz, Me of TES), 0.53 (2 x q superimposed upon one another, 6H, *J* = 8.0 Hz, -CH₂- of TES) ppm; ¹³C NMR (125 MHz, C₆D₆, 298 K) δ 210.67 (C-16), 177.19 (C=O of Piv), 174.93 (C-12), 135.73 (C-5), 120.77 (C-4), 80.37 (C-6), 68.82 (C-8), 65.48 (C-9), 59.78 (C-11), 56.82 (C-7), 38.75 (OC(O)CMe₃), 38.46 (C-17), 27.29 (OC(O)CMe₃), 22.81 (Me-13), 19.81 (Me-18 or Me-19), 19.52 (Me-18 or Me-19), 7.04 (MeCH₂- of TES), 5.41 (MeCH₂- of TES) ppm; VG 70-SE Positive Ion FAB HRMS: Calcd. for C₂₄H₄₂NaO₆Si (M+Na)⁺: 477.26482. Found: 477.26381.

Bicyclic Furanoside **31** (II-YL-161)

A mixture of β -ketoester **30** (200 mg, 0.44 mmol), pyridine *p*-toluenesulfonate (11 mg, 0.044 mmol, 0.1 equiv), trimethyl orthoformate (2 mL) and MeOH (8 mL) were heated at reflux for 48 h whereupon TLC analysis revealed that a single slower-moving major product had formed and unreacted **30** was also present. The solvents were evaporated under reduced pressure and the residue was purified by SiO₂ flash chromatography with petrol:Et₂O (7:1) as eluent. Initially, **30** (46 mg, 23%) was isolated followed by methyl furanoside **31** (0.116 g, 74%); both were colorless oils.

Data for **31**: [α]_D -50.99 ° (*c* 0.404, CH₂Cl₂); IR (KBr) 2976 (s), 2936 (m), 1774 (s), 1732 (s), 1464 (w), 1391 (w), 1366 (w), 1281 (m), 1223 (w), 1155 (s), 1092 (s), 1049 (m), 1016 (s), 935 (w) cm⁻¹; ¹H NMR (500 MHz, C₆D₆, 298 K) δ 5.56 (ddd, 1H, *J* = 6.6, 10.4, 17.1 Hz, H-5), 5.11 (ddd, 1H, *J* = 1.2, 1.2, 17.1 Hz, H-4b), 4.90 (ddd, 1H, *J* = 1.1, 10.4 Hz, H-4a), 4.50 (m, 1H, H-6), 4.02 (dd, 1H, *J* = 5.4, 11.5 Hz, H-9a), 3.88 (dd, 1H, *J* = 5.5, 11.5 Hz, H-9b), 3.80 (m, 1H, H-8), 2.99 (s, 3H, OMe), 2.13 (dd, 1H, *J* = 3.7, 7.6 Hz, H-7), 2.00 (septet,

1H, $J = 7.2$ Hz, H-17), 1.17 (d, 3H, $J = 7.0$ Hz, Me-18 or Me-19), 1.12 (d, 3H, $J = 7.1$ Hz, Me-18 or Me-19) superimposed upon 1.12 (s, 9H, OC(O)CMe₃), 1.119 (s, 3H, Me-13) ppm; ¹³C NMR (125 MHz, C₆D₆, 298 K) δ 177.46 (C=O of Piv), 174.99 (C-12), 136.79 (C-5), 117.04 (C-4), 111.82 (C-16), 83.39 (C-6), 79.42 (C-8), 65.41 (C-9), 61.51 (C-11), 59.65 (C-7), 49.66 (OMe), 38.78 (OC(O)CMe₃), 31.90 (C-17), 27.23 (OC(O)CMe₃), 21.63 (C-13), 18.53 (Me-18 or Me-19), 17.09 (Me-18 or Me-19) ppm; VG 70-SE Positive Ion FAB HRMS: Calcd. for C₁₉H₃₀NaO₆ (M+Na)⁺: 377.19400. Found: 377.19432.

Alcohol 6 (II-YL151)

A pre-prepared solution of Na (26 mg, 1.13 mmol, 2 equiv) in dry MeOH (5 mL) under N₂ was added to a round-bottomed flask containing the O-pivalate **31** (0.2 g, 0.564 mmol) at rt. The reactants were stirred for 24 h before being diluted with CH₂Cl₂ (30 mL) and filtered through a short plug of SiO₂ gel. After concentration of the filtrate *in vacuo*, the residue was purified by SiO₂ flash chromatography with petrol:EtOAc (3:1) to give alcohol **6** (0.153 g, 98%) as a white amorphous solid.

Data for **6**: [α]_D -71.6 ° (*c* 0.282, CH₂Cl₂); IR (KBr) 3416 (s), 2966 (m), 2930 (m), 1747 (s), 1466 (w), 1412 (w), 1281 (m), 1240 (m), 1146 (m), 1090 (s), 1057 (s), 1013 (s), 935 (m) cm⁻¹; ¹H NMR (500 MHz, C₆D₆, 298 K) δ 5.57 (ddd, 1H, $J = 6.3, 10.5, 17.0$ Hz, H-5), 5.12 (ddd, 1H, $J = 1.3, 1.3, 17.2$ Hz, H-4b), 4.89 (ddd, 1H, $J = 1.2, 10.5$ Hz, H-4a), 4.51 (m, 1H, H-6), 3.58 (dd, 1H, $J = 4.3, 8.5$ Hz, H-8), 3.28 (br m, 1H, H-9a), 3.18 (br m, 1H, H-9b), 3.01 (s, 3H, OMe), 2.23 (dd, 1H, $J = 3.8, 7.6$ Hz, H-7), 1.99 (septet, 1H, $J = 7.1$ Hz, H-17), 1.23 (br m, 1H, OH-9), 1.20 (d, 3H, $J = 7.0$ Hz, Me-18 or Me-19), 1.15 (s, 3H, Me-13), 1.12 (d, 3H, $J = 7.2$ Hz, Me-18 or Me-19) ppm; ¹³C NMR (125 MHz, C₆D₆, 298 K) δ 175.52 (C-12), 136.96 (C-5), 116.40 (C-4), 111.84 (C-16), 83.56 (C-6), 82.54 (C-8), 63.96 (C-9), 61.63 (C-11), 58.86 (C-7), 49.72 (OMe), 31.99 (C-17), 21.34 (C-13), 18.74 (Me-18 or Me-19), 17.17 (Me-18 or Me-19) ppm; VG 70-SE Positive Ion FAB HRMS: Calcd. for C₁₄H₂₂NaO₅ (M+Na)⁺: 293.13649. Found: 293.13724.

Preparation of O-Triflate Ester **3** and Its Alkylative Union with 3(2H)-Dihydrofuranone **2**⁵ to Obtain **32** (III-YL-17a) and **33** (III-YL-17b)

Part (i). Formation of O-Triflate Ester 3. To a stirred -78 °C solution of alcohol **6** (150 mg, 0.555 mmol) in dry CH₂Cl₂ (5 mL) under N₂ was added Et₃N (0.31 mL, 2.22 mmol). Triflic anhydride (0.187 mL, 1.11 mmol) was then added dropwise over 5 min, and the reactants were stirred at -78 °C for 15 min. H₂O (2 mL) was added followed by Et₂O (15 mL). The organic layer was separated, dried over MgSO₄, filtered and evaporated. The residue was purified by SiO₂ flash chromatography with petrol/EtOAc (3:1) to give the unstable O-triflate **3** (230 mg) as a colorless oil that was used immediately for the next step.

Part (ii). Alkylation of O-Triflate Ester 3 with 3(2H)-Dihydrofuranone 2⁵ to Obtain 32 and 33. To a stirred -78 °C solution of **2⁵** (1.40 g, 11.1 mmol, 20 equiv) in dry PhMe (5 mL) under N₂ was added KN(SiMe₃)₂ (0.5 M solution in PhMe, 22.2 mL, 11.1 mmol, 20 equiv) dropwise over 20 min. The resulting solution was stirred at -78 °C for 0.5 h whereafter a solution of **3** (230 mg, 0.555 mmol) in dry PhMe (2 mL) was added dropwise over 2 min. The reactants were gradually warmed to 0 °C over 2 h whereupon sat. aq. NH₄Cl (1 mL) was added. Following dilution with EtOAc (15 mL), the organic layer was separated, washed with H₂O (3 mL), brine (3 mL), and then dried over MgSO₄. After filtration and evaporation of the solvents *in vacuo*, purification of the residue by SiO₂ flash chromatography (4:1 petrol:EtOAc) followed by preparative TLC (4:1 petrol:EtOAc) gave **32** and **33** (171 mg, 81%) as essentially a 1:1 mixture of C(10)-epimers that appeared chromatographically homogenous according to single-elution TLC analysis.

The two epimers could only be separated by multiple-elution preparative TLC (petrol/EtOAc 4:1) on several TLC plates with recycling of the separated mixed fractions. By this method, after further final purification of the residue by SiO₂ flash chromatography (4:1 petrol:EtOAc) the faster-moving product **32** (71 mg, 34%) was isolated as an oil; the slower-moving product **33** (79 mg, 38%) was also obtained as a colorless oil. The characterisation data for these two molecules is listed below.

Data for **32**: [α]_D -135.5 ° (c 0.42, CH₂Cl₂); IR 2964 (m), 1773 (m), 1699 (m), 1593 (m), 1556 (w), 1385 (w), 1261 (s), 1090 (s), 1018 (s), 800 (s) cm⁻¹; ¹H NMR (500 MHz, C₆D₆, 298 K) δ 5.61 (ddd, 1H, *J* = 6.6, 10.4, 17.1 Hz, H-5), 5.16 (s, 1H, H-2), 5.15 (ddd, 1H, *J* = 1.2, 1.2, 17.1 Hz, H-5'a), 4.89 (ddd, 1H, *J* = 1.1, 1.1, 10.4 Hz, H-5'b), 4.58 (dd, 1H, *J* = 6.9, 7.0, H-6), 3.98 (ddd, 1H, *J* = 3.8, 3.8, 7.9 Hz, H-8), 2.97 (s, 3H, OMe), 2.03-1.90 (complex m, 5H, H-17, H-4a, H-4b, H-7, H-9a), 1.63 (dd, 1H, *J* = 3.7, 14.9 Hz, H-9b), 1.29 (s, 3H, Me-14), 1.19 (d, 3H, *J* = 7.0 Hz, Me-18 or Me-19), 1.10 (d, 3H, *J* = 7.2 Hz, Me-18 or Me-19), 1.08 (s, 3H, Me-13), 0.74 (t, 3H, *J* = 7.6 Hz, Me-15); ¹³C NMR (125 MHz, C₆D₆, 298 K) δ 204.79 (C-1), 192.46 (C-3), 175.16 (C-12), 137.14 (C-5), 116.72 (C-5'), 111.83 (C-16), 101.09 (C-2), 89.13 (C-10), 83.43 (C-6), 78.33 (C-8), 63.68 (C-7), 61.23 (C-11), 49.53 (OMe), 42.86 (C-9), 31.98 (C-17), 24.03 (C-4), 21.92 (C-14), 21.88 (C-13), 18.65 (C-18 or C-19), 17.09 (C-18 or C-19), 10.04 (C-15); VG 70-SE Positive Ion FAB HRMS: Calcd. for C₂₁H₃₀NaO₆ (M+Na)⁺: 401.19400. Found: 401.19457. The stereochemical integrity of **32** was proven by its chemical conversion into **43** (by successive treatment with OsO₄/NaIO₄ and NaBH₄) and 400 MHz ¹H NMR comparison with Tadano's spectrum for this compound.^{2b}

Data for **33**: $[\alpha]_D -26.7^\circ$ (c 0.296, CH_2Cl_2); IR 2976 (m), 2937 (m), 1773 (s), 1705 (s), 1599 (s), 1454 (w), 1379 (m), 1258 (w), 1223 (w), 1155 (s), 1124 (m), 1088 (s), 1051 (s), 1015 (s), 926 (m), 810 (w) cm^{-1} ; ^1H NMR (500 MHz, C_6D_6 , 298 K) δ 5.50 (ddd, 1H, J = 6.6, 10.4, 17.1 Hz, H-5), 5.21 (s, 1H, H-2), 5.06 (ddd, 1H, J = 1.2, 1.2, 17.1 Hz, H-5'a), 4.86 (ddd, 1H, J = 1.1, 1.1, 10.4 Hz, H-5'b), 4.55 (br dd, 1H, J = 7.0, 7.0, H-6), 3.96 (ddd, 1H, J = 2.9, 2.8, 10.6 Hz, H-8), 3.01 (s, 3H, OMe), 2.02 (septet, 1H, J = 7.2 Hz, H-17), 1.96 (dd, 1H, J = 10.6, 14.3 Hz, H-9a), 1.94 (qd, 2H, J = 0.8, 7.5 Hz, H-4a, H-4b), 1.85 (dd, 1H, J = 3.8, 7.5 Hz, H-7), 1.59 (dd, 1H, 2.6, 14.4 Hz, H-9b), 1.25 (s, 3H, Me-14), 1.22 (d, 3H, J = 7.0 Hz, Me-18 or Me-19), 1.14 (d, 3H, J = 7.2 Hz, Me-18 or Me-19), 1.12 (s, 3H, Me-13), 0.77 (t, 3H, J = 7.5 Hz, Me-15); ^{13}C NMR (125 MHz, C_6D_6 , 298 K) δ 204.30 (C-1), 190.62 (C-3), 175.18 (C-12), 137.13 (C-5), 116.66 (C-5'), 112.23 (C-16), 101.66 (C-2), 87.80 (C-10), 83.40 (C-6), 76.90 (C-8), 63.09 (C-7), 61.31 (C-11), 49.78 (OMe), 43.36 (C-9), 32.13 (C-17), 23.85 (C-4), 23.23 (C-14), 21.87 (C-13), 18.77 (C-18 or C-19), 17.00 (C-18 or C-19), 10.19 (C-15); VG 70-SE Positive Ion FAB HRMS: Calcd. for $\text{C}_{21}\text{H}_{30}\text{NaO}_6$ ($\text{M}+\text{Na}$) $^+$: 401.19400. Found: 401.19455. The structural integrity of **33** was proven by its chemical conversion into **4** and (+)-eremantholide A and our $^1\text{H}/^{13}\text{C}$ NMR correlations with Tadano's spectra and his reported spectral data for these two compounds.

Whilst the separation of **32** and **33** could successfully be effected at this stage, and the purified molecules individually taken forward to alkenes **35** and **1** respectively, we have generally found it much more convenient to take the purified but unseparated mixture of **32** and **33** forward to the alkene stage and effect isomer separation at that point. Accordingly, we now present the optimised procedures for securing **35** and **1** from the 1:1 mixture of **32/33**.

Preparation of **1** (III-YL-37b) and **35** (III-YL-26) from the Mixture of **32** and **33**

To a stirred -78°C solution of the purified but unseparated mixture of **32** and **33** (82.5 mg, 0.218 mmol) in dry THF (2 mL) under N_2 was added $\text{LiN}(\text{SiMe}_3)_2$ (1M solution in THF, 0.34 mL, 0.34 mmol, 1.56 equiv) dropwise over 2 min. Stirring was continued for 20 min whereupon a combined stream of gaseous HCHO and N_2 was passed just above the surface of the -78°C reaction mixture for 10 min. The gaseous HCHO/N_2 mixture was generated by heating solid paraformaldehyde in a two necked round bottom flask at 170°C in an oil-bath and slowly carrying it over into the reaction flask via thermally-stable, wide-bore, silicone-type tubing through application of a positive pressure of N_2 gas (**Warning: Do NOT attempt to use a metal cannula for this gaseous HCHO/N_2 transfer, NOR use a heat gun to crack the solid paraformaldehyde, as thin metal cannulae are liable to get blocked very quickly due to rapid cooling and solidification of gaseous HCHO ; the rapid cracking of $(\text{HCHO})_n$ with a heat gun is also liable to cause a dangerous pressure build-up**

within the generating apparatus, particularly when the metal cannula gets blocked with condensed HCHO, as often happens. By adhering to the experimental set-up we have described, we have not encountered any problems in generating gaseous HCHO safely). Following exposure of the reaction mixture to gaseous HCHO for 10 min, the reactants were allowed to stir for 0.5 h, and then quenched by adding saturated aqueous NH₄Cl (0.5 mL), EtOAc (10 mL) and H₂O (2 mL). The organic layer was separated, washed successively with H₂O (2 mL) and brine (2 mL), dried over MgSO₄, filtered and concentrated *in vacuo*. The residue was purified by SiO₂ flash chromatography (gradient elution with petrol/EtOAc from 2:1 to 1:2), the desired product mixture **34** (95 mg, >100%) being isolated as an oil after drying *in vacuo*; it appeared as essentially a single slower-moving product according to TLC analysis.

To a 0 °C solution of the aforementioned sample of **34** (95 mg, assumed to be 0.218 mmol) in dry THF (2 mL) under N₂ was added Et₃N (0.20 mL, 1.44 mmol, 6.6 equiv) in one portion. A solution of MsCl (0.069 mL, 0.891 mmol, 4.1 equiv) in dry THF (0.5 mL) was then added dropwise over 1 min. The reactants were stirred at 0 °C for 1 h, whereupon a solution of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) (0.2 mL, 1.34 mmol, 6.13 equiv) in dry THF (0.5 mL) was added dropwise over 1 min. Stirring was continued at 0 °C for 1 h, whereafter the reaction was quenched with saturated aqueous NaHCO₃ (5 mL). Following dilution with EtOAc (20 mL), the organic layer was separated and washed with H₂O (5 mL) and brine (5 mL), dried over MgSO₄, filtered and concentrated *in vacuo*. Purification of the residue by SiO₂ flash chromatography with petrol/EtOAc (3:1) furnished the desired alkenes **1** and **35** as mixture (59.0 mg, 69%) that moved as a single spot after single elution TLC in the aforementioned solvent system. The two components could be successfully separated by multiple-elution preparative TLC using petrol/EtOAc (4:1) as eluent. By this method, the faster moving product **35** (24 mg, 28%) and the slower-moving product **1** (27.4 mg, 32%) were both isolated as oils after further purification by SiO₂ flash chromatography using petrol/EtOAc (3:1) as eluent. Their respective characterisation data are reported below:

Data for **35**: [α]_D -119.1 ° (c 0.262, CH₂Cl₂); IR 2936 (m), 1774 (s), 1697 (s), 1634 (m), 1560 (s), 1452 (w), 1373 (m), 1263 (m), 1123 (s), 1088 (m), 1051 (m), 1016 (m), 934 (w), 812 (w) cm⁻¹; ¹H NMR (500 MHz, C₆D₆, 298 K) δ 5.81 (br s, 1H, H-4'a), 5.60 (ddd, 1H, *J* = 6.5, 10.4, 17.0 Hz, H-5), 5.38 (s, 1H, H-2), 5.15 (ddd, 1H, *J* = 1.2, 1.2, 17.1 Hz, H-5'a), 4.93 (m, 1H, H-4'b), 4.88 (ddd, 1H, *J* = 1.1, 1.1, 10.4 Hz, H-5'b), 4.58 (br m, 1H, H-6), 3.97 (ddd, 1H, *J* = 3.8, 4.0, 7.9, 8.8 Hz, H-8), 2.97 (s, 3H, OMe), 2.04-1.92 (complex m, 3H, H-7, H-9a, H-17), 1.71 (dd, 1H, *J* = 3.7, 14.8 Hz, H-9b), 1.51 (narrow dd resembling a singlet, 3H, *J* = 0.9, 1.3 Hz, Me-15), 1.29 (s, 3H, Me-14), 1.19 (d, 3H, *J* = 7.0 Hz, Me-18 or Me-19), 1.08 (d, 3H, *J* = 7.2 Hz, Me-18 or Me-19) superimposed upon 1.078 (s, 3H, Me-13); ¹³C NMR (125 MHz, C₆D₆, 298 K) δ 204.98 (C-1), 183.17 (C-3), 175.16 (C-12), 137.10 (C-5), 134.04 (C-4), 120.76 (C-4'), 116.70 (C-5'), 111.82 (C-16), 101.24 (C-2), 89.22 (C-10), 83.44 (C-6), 78.42 (C-8), 63.60 (C-7), 61.25 (C-11), 49.54 (OMe), 43.09 (C-9), 32.01 (C-17), 22.24 (C-14), 21.92 (C-13), 18.66 (C-18 or C-19), 18.48 (C-15), 17.12 (C-18 or C-19); VG 70-SE Positive Ion FAB HRMS: Calcd. for C₂₂H₃₀NaO₆ (M+Na)⁺: 413.19400. Found: 413.19337.

Data for **1**: [α]_D -22.9 ° (c 0.35, CH₂Cl₂); IR 2970 (m), 2928 (m), 1773 (s), 1701 (s), 1634 (m), 1562 (s), 1454 (w), 1371 (m), 1329 (w), 1259 (m), 1108 (s), 1013 (s), 957 (m), 934 (m) cm⁻¹; ¹H NMR (500 MHz, C₆D₆, 298 K) δ 5.80 (br s, 1H, H-4'a), 5.48 (ddd, 1H, *J* = 6.7, 10.4, 17.1 Hz, H-5), 5.45 (s, 1H, H-2), 5.04 (ddd, 1H, *J* =

1.2, 1.2, 17.1 Hz, H-5'a), 4.91 (m, 1H, H-4'b), 4.84 (ddd, 1H, $J = 1.1, 1.1, 10.4$ Hz, H-5'b), 4.52 (dd, 1H, $J = 7.0, 7.0$ Hz, H-6), 3.99 (ddd, 1H, H-8), 2.99 (s, 3H, OMe), 2.02 (septet, 1H, $J = 7.2$ Hz, H-17) superimposed upon 2.00 (dd, 1H, $J = 14.3, 14.4$ Hz, H-9a), 1.85 (dd, 1H, $J = 3.9, 7.4$ Hz, H-7), 1.64 (dd, 1H, $J = 2.7, 14.3$ Hz, H-9b), 1.52 (large narrow dd that resembles a s, 3H, $J = 0.9, 1.3$ Hz, Me-15), 1.26 (s, 3H, Me-14), 1.22 (d, 3H, $J = 7.0$ Hz, Me-18 or Me-19), 1.13 (d, 3H, $J = 7.2$ Hz, Me-18 or Me-19), 1.11 (s, 3H, Me-13); ^{13}C NMR (125 MHz, C_6D_6 , 298 K) δ 204.54 (C-1), 181.48 (C-3), 175.16 (C-12), 137.14 (C-5), 134.08 (C-4), 119.77 (C-4'), 116.61 (C-5'), 112.19 (C-16), 101.97 (C-2), 87.83 (C-10), 83.41 (C-6), 77.06 (C-8), 62.96 (C-7), 61.38 (C-11), 49.66 (OMe), 43.64 (C-9), 32.08 (C-17), 23.31 (C-14), 21.92 (C-13), 18.77 (C-18 or C-19), 18.53 (C-15), 16.99 (C-18 or C-19); VG 70-SE Positive Ion FAB HRMS: Calcd. for $\text{C}_{22}\text{H}_{30}\text{NaO}_6$ ($\text{M}+\text{Na}$) $^+$: 413.19400. Found: 413.19298.

(+)-16-Methoxy-Eremantholide A (III-YL-38)

A solution of **1** (20 mg, 0.0512 mmol) and the Hoveyda type II RCM catalyst **36** (6.4 mg, 0.0102 mmol, 0.2 equiv) in dry PhMe (50 mL) was heated at reflux for 14 h. After this time, TLC analysis (petrol/EtOAc 2:1) revealed that a slightly faster-moving product **4** had formed together with a much slower-moving cross metathesis product **44**. At this juncture, the solvent was removed *in vacuo* and the crude residue was purified by multiple-elution preparative TLC using petrol/EtOAc (3:1) as eluent. The desired product **4** (10 mg, 54%) was isolated as a colorless oil following SiO_2 flash chromatography of the concentrated residue using the same eluent. The cross-metathesis product **44** was typically isolated in about 15% yield on the various runs in which the yield of this undesired by-product was quantified.

Data for **4**: $[\alpha]_{\text{D}} +21.4^\circ$ (c 0.168, CHCl_3); IR 2976 (m), 2928 (m), 1776 (s), 1709 (s), 1659 (m), 1587 (s), 1450 (w), 1369 (m), 1288 (m), 1134 (s), 1099 (s), 1057 (s), 1013 (s), 910 (m) 735 (m) cm^{-1} ; ^1H NMR (500 MHz, CDCl_3 , 298 K) δ 5.97 (m, 1H, H-5), 5.58 (s, 1H, H-2), 4.71 (m, 1H, H-6), 3.70 (ddd, 1H, $J = 2.6, 4.1, 11.7$ Hz, H-8), 3.19 (s, 3H, OMe), 2.75 (dd, 1H, $J = 4.2, 7.2$ Hz, H-7), 2.35 (dd, 1H, $J = 2.5, 13.6$ Hz, H-9a), 2.08 (septet, 1H, $J = 7.1$ Hz, H-17), 2.02 (m, H-9b) superimposed upon 2.02 (s, 3H, Me-15), 1.47 (s, 3H, Me-14), 1.28 (s, 3H, Me-13), 1.09 (d, 3H, $J = 7.3$ Hz, Me-18 or Me-19), 1.07 (d, 3H, $J = 7.1$ Hz, Me-18 or Me-19); ^{13}C NMR (125 MHz, CDCl_3 , 298 K) δ 205.18 (C-1), 186.85 (C-3), 175.86 (C-12), 134.74 (C-5), 129.96 (C-4), 109.97 (C-16), 104.41 (C-2), 89.90 (C-10), 81.49 (C-6), 78.43 (C-8), 63.85 (C-7), 62.28 (C-11), 50.01 (OMe), 43.95 (C-9), 31.15 (C-17), 22.25 (C-13), 20.54 (C-14), 20.38 (C-15), 18.46 (C-18 or C-19), 16.71 (C-18 or C-19).

19); VG 70-SE Positive Ion FAB HRMS: Calcd. for $C_{20}H_{27}O_6$ (M+H)⁺: 363.18075. Found: 363.17937. Our spectra and spectral data for **4** correlated well with the spectra and data reported for **4** by Tadano *et al.*^{2b}

(+)-Eremantholide A (III-YL-39)

(+)-16-Methoxy-eremantholide A **4** (5.1 mg, 0.0141 mmol) was treated with an 8:1 v/v mixture of THF: 6 M aqueous HCl (1 mL) at rt for 16 h. Solid $NaHCO_3$ was then added to neutralise the excess aqueous HCl, and EtOAc (10 mL) was added followed by H_2O (5 mL). The organic layer was separated and washed with H_2O (5 mL) and brine (5 mL), dried over $MgSO_4$, filtered and concentrated *in vacuo*. The residue was purified by preparative TLC using EtOAc/petrol (1:3) as eluent. Further final purification was effected by SiO_2 flash chromatography with the same eluent. Our synthetic (+)-eremantholide A (4.0 mg, 82%) was obtained as an amorphous white solid; its spectra and spectral properties matched those reported by Tadano *et al.*^{2b}

Data for synthetic **(+)-Eremantholide A**: $[\alpha]_D^{25} +38.8^\circ$ (*c* 0.08, EtOH) [Lit.^{2b}: $[\alpha]_D^{25} +68.8^\circ$ (*c* 0.18, EtOH)]; 1H NMR (500 MHz, $CDCl_3$, 298 K) δ 5.99 (m, 1H, H-5), 5.57 (s, 1H, H-2), 4.93 (m, 1H, H-6), 4.02 (ddd, 1H, *J* = 2.6, 4.2, 11.8 Hz, H-8), 2.78 (dd, 1H, *J* = 4.2, 7.3 Hz, H-7), 2.28 (dd, 1H, *J* = 2.5, 13.6 Hz, H-9a) superimposed upon 2.27 (s, C-16 OH), 2.03 (dd, 3H, *J* = 2.2, 1.8 Hz, Me-15), 1.98 (dd, 1H, *J* = 13.6, 13.5 Hz, H-9b) superimposed upon 1.99 (septet, 1H, H-17), 1.46 (s, 3H, Me-14), 1.30 (s, 3H, Me-13), 1.04 (d, 3H, *J* = 6.9 Hz, Me-18 or Me-19), 0.93 (d, 3H, *J* = 6.8 Hz, Me-18 or Me-19); ^{13}C NMR (125 MHz, $CDCl_3$, 298 K) δ 205.31 (C-1), 186.84 (C-3), 175.52 (C-12), 134.69 (C-5), 130.00 (C-4), 107.78 (C-16), 104.46 (C-2), 89.94 (C-10), 81.34 (C-6), 77.87 (C-8), 63.54 (C-7), 60.08 (C-11), 43.84 (C-9), 32.00 (C-17), 21.02 (C-13), 20.50 (C-14), 20.37 (C-15), 16.77 (C-18 or C-19), 16.56 (C-18 or C-19); VG 70-SE Positive Ion FAB HRMS: Calcd. for $C_{19}H_{25}O_6$ (M+H)⁺: 349.16511. Found: 349.16412.

Intersection with Tadano's Synthesis; A New Formal Asymmetric Total Synthesis of (+)-Eremantholide A

Alcohol 37 (III-YL-45)

A stream of gaseous O₃ was bubbled into a -78 °C solution of alkene **31** (20 mg, 0.056 mmol) in MeOH/CH₂Cl₂ (2:1) (3 mL) until a slightly blue color appeared. Whilst maintaining the reaction mixture at -78 °C, NaBH₄ (21 mg, 0.56 mmol) was added in one portion and, after 5 min, the reaction mixture was allowed to warm to 0 °C. A second portion of NaBH₄ (21 mg, 0.56 mmol) was added and stirring was continued at 0 °C for 1 h. EtOAc (30 mL) was then added and the mixture was passed through a short column of SiO₂ gel which was later washed thoroughly with EtOAc. Following concentration of the solvents *in vacuo*, the residue was purified by SiO₂ flash chromatography (petrol/EtOAc 3:1) whereafter **37** (16 mg, 79%) was obtained as a colorless oil.

Data for **37**: [α]_D -41.1 ° (c 0.246, CH₂Cl₂); IR 3467 (br m), 2941 (s), 1771 (s), 1734 (s), 1460 (m), 1371 (m), 1283 (s), 1244 (m), 1161 (s), 1092 (s), 1051 (s), 1020 (s), 907 (m) cm⁻¹; ¹H NMR (500 MHz, CDCl₃, 298 K) δ 4.35 (ddd, 1H, *J* = 3.5, 3.8, 7.3 Hz, H-6), 4.19 (m, 1H, H-9a), 4.08 (complex m, 2H, H-8, H-9b), 3.83 (br m, H-5a), 3.57 (m, 1H, H-5b), 3.30 (s, 3H, OMe), 2.62 (dd, 1H, *J* = 3.9, 7.0 Hz, H-7), 2.16 (septet, 1H, *J* = 7.2 Hz, H-17), 2.06 (br t, 1H, OH-5), 1.35 (s, 3H, Me-13), 1.20 (s, 9H, OC(O)CMe₃), 1.13 (d, 3H, *J* = 7.2 Hz, Me-18 or Me-19), 1.09 (d, 3H, *J* = 7.0 Hz, Me-18 or Me-19) ppm; ¹³C NMR (125 MHz, CDCl₃, 298 K) δ 178.31 (C=O of Piv), 176.44 (C-12), 111.66 (C-16), 83.23 (C-6), 79.72 (C-8), 65.27 (C-9), 63.21 (C-5), 61.95 (C-11), 54.30 (C-7), 49.87 (OMe), 38.82 (OC(O)CMe₃), 31.48 (C-17), 27.18 (OC(O)CMe₃), 21.05 (C-13), 18.29 (Me-18 or Me-19), 16.83 (Me-18 or Me-19) ppm; VG 70-SE Positive Ion FAB HRMS: Calcd. for C₁₈H₃₀NaO₇ (M+Na)⁺: 381.18891. Found: 381.18794.

Pivaloate **38** (III-YL-46)

To a stirred rt solution of alcohol **37** (20 mg, 0.0558 mmol) in dry DMF (1 mL) under N₂ was successively added imidazole (11 mg, 0.162 mmol) and *t*-BuPh₂SiCl (0.022 mL, 0.0846 mmol) in single portions. The reaction mixture was stirred for 4 h, whereafter it was diluted with Et₂O (20 mL) and washed with H₂O (2 x 2 mL), brine (2 mL) and dried over MgSO₄. After filtration and concentration *in vacuo*, the residue was purified by SiO₂ flash chromatography to give **38** (28 mg, 84%) as a colorless oil.

Data for **38**: [α]_D -17.5 ° (c 0.228, CH₂Cl₂); IR 2936 (s), 2862 (m), 1773 (s), 1732 (s), 1470 (m), 1431 (w), 1391 (w), 1367 (w), 1281 (w), 1157 (s), 1113 (s), 1057 (s), 1018 (m), 939 (w), 704 (s) cm⁻¹; ¹H NMR (500 MHz, CDCl₃, 298 K) δ 7.66-7.59 (m, 4H, Ph), 7.45-7.34 (m, 6H, Ph), 4.28 (partially overlapped ddd, 1H, *J* = 3.5, 3.4, 6.9 Hz, H-6), 4.14-4.06 (m, 2H, H-9a, H-9b), 4.01 (dd, 1H, *J* = 4.4, 8.9 Hz, H-8), 3.82 (dd, 1H, *J* = 3.7, 11.4 Hz, H-5a), 3.63 (dd, 1H, *J* = 3.5, 11.4 Hz, H-5b), 3.28 (s, 3H, OMe), 2.75 (dd, 1H, *J* = 4.3, 6.8 Hz,

H-7), 2.17 (septet, 1H, $J = 7.2$ Hz, H-17), 1.38 (s, 3H, Me-13), 1.16 (s, 9H, OC(O)CMe₃), 1.14 (d, 3H, $J = 7.2$ Hz, Me-18 or Me-19), 1.11 (d, 3H, $J = 7.1$ Hz, Me-18 or Me-19), 1.03 (s, 9H, *t*-BuPh₂Si-) ppm; ¹³C NMR (125 MHz, CDCl₃, 298 K) δ 178.18 (C=O of Piv), 176.20 (C-12), 135.69 (Ph), 135.50 (Ph), 132.85 (Ph), 132.41 (Ph), 129.94 (Ph), 129.93 (Ph), 127.84 (Ph), 127.82 (Ph), 111.59 (C-16), 83.03 (C-6), 79.94 (C-8), 65.11 (C-9), 64.19 (C-5), 61.93 (C-11), 53.91 (C-7), 49.74 (OMe), 38.76 (OC(O)CMe₃), 31.41 (C-17), 27.16 (OC(O)CMe₃), 26.75 (Me₃C- of *t*-BuPh₂Si-), 21.06 (C-13), 19.16 (Me₃C- of *t*-BuPh₂Si-), 18.27 (Me-18 or Me-19), 16.86 (Me-18 or Me-19) ppm; VG 70-SE Positive Ion FAB HRMS: Calcd. for C₃₄H₄₈NaO₇Si (M+Na)⁺: 619.30668. Found: 619.30708.

Tadano's Alcohol **39** (III-YL-48)

To a stirred rt solution of pivaloate **38** (28 mg, 0.047 mmol) in dry MeOH (1 mL) was added a solution of NaOMe (prepared from Na (2 mg, 0.087 mmol, 1.85 equiv) in MeOH (0.5 mL)). The reactants were stirred for 12 h, diluted with CH₂Cl₂ (15 mL) and filtered through a short column of SiO₂ gel that was washed thoroughly with CH₂Cl₂/MeOH (10:1). The filtrate was concentrated *in vacuo* and the residue was purified by SiO₂ flash chromatography with petrol/EtOAc (5:1) as eluent. The title compound **39** (22 mg, 92%) was obtained as a white solid.

Data for **39**: [α]_D -32.4 ° (*c* 0.364, CHCl₃) [Lit.^{2b}: -35.1 ° (*c* 0.92 CHCl₃)]; IR (KBr) 3555 (s br), 2934 (s), 2883 (m), 2858 (m), 1745 (s), 1466 (w), 1425 (w), 1381 (w), 1234 (m), 1109 (s), 1086 (s), 1055 (s), 974 (w), 949 (w), 808 (w), 706 (s) cm⁻¹; ¹H NMR (500 MHz, CDCl₃, 298 K) δ 7.66-7.61 (m, 4H, Ph), 7.45-7.35 (m, 6H, Ph), 4.26 (ddd, 1H, $J = 4.1, 6.9, 8.3$ Hz, H-6), 3.90 (dd, 1H, $J = 4.1, 8.6$ Hz, H-8), 3.76 (dd, 1H, $J = 4.6, 11.2$ Hz, H-5a), 3.68 (dd, 1H, $J = 3.8, 11.2$ Hz, H-5b) superimposed upon 3.72-3.64 (very br s, 1H, H-9a), 3.55 (br m, 1H, H-9b), 3.29 (s, 3H, OMe), 2.70 (dd, 1H, $J = 4.2, 6.9$ Hz, H-7), 2.15 (septet, 1H, $J = 7.2$ Hz, H-17), 1.73 (br t, 1H, OH-9), 1.31 (s, 3H, Me-13), 1.15 (d, 3H, $J = 7.2$ Hz, Me-18 or Me-19), 1.11 (d, 3H, $J = 7.0$ Hz, Me-18 or Me-19), 1.04 (s, 9H, *t*-BuPh₂Si-) ppm; ¹³C NMR (125 MHz, CDCl₃, 298 K) δ 176.40 (C-12), 135.65 (Ph), 135.57 (Ph), 132.85 (Ph), 132.60 (Ph), 2 x 129.94 (Ph), 127.83 (Ph), 127.82 (Ph), 111.71 (C-16), 82.96 (C-6), 82.80 (C-8), 64.59 (C-5), 64.03 (C-9), 61.83 (C-11), 54.08 (C-7), 49.92 (OMe), 31.56 (C-17), 26.81 (Me₃C- of *t*-BuPh₂Si-), 20.84 (C-13), 19.20 (Me₃C- of *t*-BuPh₂Si-), 18.50 (Me-18 or Me-19), 16.92 (Me-18 or Me-19) ppm; VG 70-SE Positive Ion FAB HRMS: Calcd. for C₂₉H₄₀NaO₆Si (M+Na)⁺: 535.24917. Found: 535.25002.

Asymmetric Total Synthesis and Formal Total Synthesis of the Antitumor Sesquiterpenoid (+)- Eremantholide A

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Supporting Information

Part 2. Copies of the 1D and 2D 500 MHz ^1H and 125 MHz ^{13}C NMR Spectra, the HR Mass Spectra, and the IR Spectra for the Intermediates Used in the Asymmetric Total Synthesis and Formal Total Synthesis of (+)-Eremantholide A.

II-YL-105
PROTON
CDCl₃

II-YL-105
COSY
CDCl₃

II-YL-105
NOESY
CDC13

II-YL-105
CARBON
CDCl₃

13

II-YL-105
DEPT
CDCl₃

II-YL-105
HMQC
CDCl₃

01030806: Scan Avg 162-163 (32.30 - 32.50 min) - Back
Base: 282.00 Int: 2.89053e+006 Sample: VG 70-SE Positive Ion FAB

Sample: IL-YL-105
Instrument Resolution: 7000
Theoretical Mass: (M+Na) 282.11061
Measured Mass: (M+Na) 282.11104
Error: 1.52 ppm

- II-YL-105 KBr

II-YL-101
PROTON
CDCl₃

CC(C)(COP(=O)(C)C)C(=O)O[C@@H]1C[C@H](C)N1C(=O)O

12

ppm

II-YL-101
CARBON
CDC13

12

II-YL-101
DEPT
CDCl₃

2D NMR spectrum of compound 10. The plot shows correlations between ^1H and ^{13}C chemical shifts. The ^1H spectrum is projected along the top axis (0 to 8 ppm), and the ^{13}C spectrum is projected along the left axis (10 to 140 ppm). The 2D plot shows several peaks, with the following approximate coordinates (ppm):

Label	^1H (ppm)	^{13}C (ppm)
1	~0.9	~15
2	~1.2	~30
3	~1.5	~45
4	~2.1	~65
5	~2.5	~80
6	~3.1	~115
7	~7.1	~135
8	~7.2	~138
9	~7.3	~139
10	~7.4	~140

02020806: Scan Avg 265-267 (52.90 - 53.30 min) - Back
Base: 580.00 Int: 2.40415e+006 Sample: VG 70-SE Positive Ion FAB

12

Sample: II-YL-101
Instrument Resolution: 7000
Theoretical Mass: (M+Na) 580.24951
Measured Mass: (M+Na) 580.24990
Error: 0.67 ppm

II-YL-46
PROTON
CDCl₃

II-YL-46
COSY
CDCl₃

II-YL-46
NOESY
CDCl₃

II-YL-46
CARBON
CDCl₃

II-YL-46
DEPT
CDCl₃

2D NMR spectrum of compound 10a. The x-axis represents ^1H chemical shift (ppm) from 0 to 8. The y-axis represents ^{13}C chemical shift (ppm) from 20 to 140. The spectrum displays several cross-peaks, with the following labels indicating specific assignments:

- 1: Aromatic region, ^1H ~7.2 ppm, ^{13}C ~135 ppm.
- 2: Aromatic region, ^1H ~7.5 ppm, ^{13}C ~130 ppm.
- 3: Aromatic region, ^1H ~7.8 ppm, ^{13}C ~125 ppm.
- 4: Aromatic region, ^1H ~7.5 ppm, ^{13}C ~120 ppm.
- 5: Aromatic region, ^1H ~7.2 ppm, ^{13}C ~115 ppm.
- 6: Aromatic region, ^1H ~7.0 ppm, ^{13}C ~110 ppm.
- 7: Aromatic region, ^1H ~6.8 ppm, ^{13}C ~105 ppm.
- 8: Aromatic region, ^1H ~6.5 ppm, ^{13}C ~100 ppm.
- 9: Aromatic region, ^1H ~6.2 ppm, ^{13}C ~95 ppm.
- 10: Aromatic region, ^1H ~6.0 ppm, ^{13}C ~90 ppm.

02020806: Scan 280 (55.90 min) - Back
Base: 173.00 Int: 5.34178e+006 Sample: VG 70-SE Positive Ion FAB

Sample: II-YL-46
Instrument Resolution: 7000
Theoretical Mass (M+Na): 407.20183
Measured Mass (M+Na): 407.20203
Error: 0.49 ppm

II-YL-47
PROTON
CDCl₃

II-YL-47
COSY
CDCl₃

II-YL-47
NOESY
CDC13

II-YL-47
CARBON
CDCl₃

II-YL-47
DEPT
CDCl₃

II-YL-47
HMQC
CDCl₃

y1 #190 RT: 8.79 AV: 1 SB: 32 0.09-0.87, 0.78-1.38 NL: 1.72E5
T: + c ESI Full ms [139.50-1000.50]

Sample: II-YL-47

Instrument Resolution: 6142

Theoretical Mass: (M+H) 147.10157

Measured Mass: (M+H) 147.10194

Error: 2.52 ppm

II-YL-53
PROTON
CDCl₃

II-YL-53
COSY
CDCl₃

II-YL-53
NOESY
CDCl₃

II-YL-53
CARBON
CDCl₃

II-YL-53
DEPT
CDCl₃

II-YL-53
HMQC
CDCl₃

01030806: Scan Avg 194-197 (38.70 - 39.30 min) - Back
Base: 173.00 Int: 5.35204e+006 Sample: VG 70-SE Positive Ion FAB

Sample: II-YL-53
Instrument Resolution: 7000
Theoretical Mass: (M+Na) 249.14666
Measured Mass: (M+Na) 249.14687
Error: 0.84 ppm

II-YL-61
 PROTON
 CDCL3

II-YL-61
COSY
CDC13

18

II-YL-61
NOESY
CDCl₃

18

II-YL-61
CARBON
CDC13

18

II-YL-61
DEPT
CDCl₃

II-YL-61
HMQC
CDCl₃

18

01030806: Scan Avg 173-175 (34.50 - 34.90 min) - Back
Base: 173.00 Int: 1.16896e+006 Sample: VG 70-SE Positive Ion FAB

Sample: II-YL-61
Instrument Resolution: 7000
Theoretical Mass: (M+Na) 353.17287
Measured Mass: (M+Na) 353.17187
Error: 2.83 ppm

II-YL-158
PROTON
CDCl₃

II-YL-158
COSY
CDCl₃

II-YL-158
NOESY
CDC13

II-YL-158
CARBON
CDCl₃

19

II-YL-158
DEPT
CDCl₃

II-YL-158
HMQC
CDCl₃

01030806: Scan Avg 183-184 (36.50 - 36.70 min) - Back
Base: 173.00 Int: 1.89719e+006 Sample: VG 70-SE Positive Ion FAB

Sample: IL-YL-158
Instrument Resolution: 7000
Theoretical Mass: (M+Na) 357.16778
Measured Mass: (M+Na) 357.16823
Error: 1.26 ppm

II-YL-122
 PROTON
 CDCl₃

II-YL-122
COSY
CDCl₃

II-YL-122
NOESY
CDC13

II-YL-122
CARBON
CDCl₃

20

II-YL-122
DEPT
CDC13

II-YL-122
HMQC
CDCl₃

02020806: Scan Avg 314-316 (62.70 - 63.10 min) - Back
Base: 595.00 Int: 442497 Sample: VG 70-SE Positive Ion FAB

Sample: II-YL-122
Instrument Resolution: 7000
Theoretical Mass: (M+Na) 595.28556
Measured Mass: (M+Na) 595.28414
Error: 2.39 ppm

II-YL-125
PROTON
CDC13

II-YL-125
COSY
CDC13

II-YL-125
NOESY
CDC13

21

II-YL-125
CARBON
CDCl₃

21

II-YL-125
DEPT
CDCl₃

II-YL-125
HMQC
CDCl₃

02020806: Scan Avg 294-298 (58.70 - 59.50 min) - Back
Base: 176.00 Int: 1.28651e+006 Sample: VG 70-SE Positive Ion FAB

Sample: II-YL-125
Instrument Resolution: 7000
Theoretical Mass (M+Na): 491.25934
Measured Mass (M+Na): 491.25812
Error: 2.48 ppm

21

II-YL-166
PROTON
C6D6

OTBDPS

23

Chemical structure of compound 23: CCCC(=O)C[C@@H]1C[C@H](C1)O[C@H]2CCCC2

1H NMR spectrum (CDCl₃) of compound 23. The x-axis represents chemical shift in ppm, ranging from 0 to 10. The spectrum shows several peaks: a broad peak around 9.8 ppm (aldehyde proton), a multiplet between 7.0 and 8.0 ppm (aromatic protons), a multiplet between 4.0 and 5.0 ppm (sugar ring protons), and a multiplet between 3.0 and 4.0 ppm (side chain protons). The inset shows a zoomed-in view of the 3.6-4.4 ppm region, highlighting the side chain protons.

II-YL-166
COSY
C6D6

II-YL-166
NOESY
C6D6

23

II-YL-166
CARBON
C6D6

II-YL-166
DEPT
C6D6

II-YL-166
HMQC
C6D6

01100806: Scan 55 (10.90 min) - Back
Base: 489.00 Int: 3.71691e+006 Sample: VG 70-SE Positive Ion FAB

Sample: II-YL-166
Instrument Resolution: 8000
Theoretical Mass: (M+Na) 489.24369
Measured Mass: (M+Na) 489.24277
Error: 1.88 ppm

II-YL-166

II-YL-167
PROTON
C6D6

II-YL-167
COSY
C6D6

24

II-YL-167
NOESY
C6D6

II-YL-167
CARBON
C6D6

24

II-YL-167
DEPT
C6D6

II-YL-167
HMQC
C6D6

01100806: Scan 119 (23.70 min) - Back
Base: 173.00 Int: 2.85656e+006 Sample: VG 70-SE Positive Ion FAB

Sample: II-YL-167
Instrument Resolution: 8000
Theoretical Mass: (M+Na) 545.26991
Measured Mass: (M+Na) 545.26894
Error: 1.78 ppm

— II-YL-167

II-YL-168
 PROTON
 CDCl₃

II-YL-168
COSY
CDCl₃

II-YL-168
NOESY
CDCl₃

II-YL-168
DEPT
CDC13

II-YL-168
HMQC
CDCl₃

01110806: Scan Avg 122-123 (24.30 - 24.50 min) - Back
Base: 173.00 Int: 1.08996e+006 Sample: VG 70-SE Positive Ion FAB

Sample: II-YL-168
Instrument Resolution: 8000
Theoretical Mass: (M+Na) 517.27499
Measured Mass: (M+Na) 517.27390
Error: 2.11 ppm

II-YL-134
 PROTON
 CDC13

II-YL-134
COSY
CDC13

II-YL-134
NOESY
CDCl₃

II-YL-134
CARBON
CDCl₃

II-YL-134
DEPT
CDC13

II-YL-134
HMQC
CDCl₃

01100806: Scan Avg 66-68 (13.10 - 13.50 min) - Back
Base: 221.00 Int: 1.99442e+006 Sample: VG 70-SE Positive Ion FAB

Sample: II-YL-134
Instrument Resolution: 8000
Theoretical Mass: (M+Na) 533.26991
Measured Mass: (M+Na) 533.27059
Error: 1.28 ppm

II-YL-136
 PROTON
 C6D6

II-YL-136
COSY
C6D6

II-YL-136
NOESY
C6D6

II-YL-136
CARBON
C6D6

II-YL-136
DEPT
C6D6

II-YL-136
HMQC
C6D6

01100806: Scan Avg 100-105 (19.90 - 20.90 min) - Back
Base: 173.00 Int: 3.48265e+006 Sample: VG 70-SE Positive Ion FAB

Sample: II-YL-136
Instrument Resolution: 8000
Theoretical Mass: (M+Na) 643.17164
Measured Mass: (M+Na) 643.17024
Error: 2.18 ppm

II-YL-137
 PROTON
 CDCl₃

II-YL-137
COSY
CDCl₃

II-YL-137
NOESY
CDC13

II-YL-137
CARBON
CDC13

II-YL-137
DEPT
CDC13

II-YL-137
 HMQC
 CDCl₃

01030806: Scan Avg 151-153 (30.10 - 30.50 min) - Back
Base: 173.00 Int: 2.61501e+006 Sample: VG 70-SE Positive Ion FAB

Sample: II-YL-137

Instrument Resolution: 7000

Theoretical Mass: (M+Na) 517.27499

Measured Mass: (M+Na) 517.27438

Error: 01.18 ppm

II-YL-138
PROTON
CDC13

II-YL-138
COSY
CDC13

II-YL-138
NOESY
CDC13

II-YL-138
CARBON
CDCl₃

II-YL-138
DEPT
CDCl₃

II-YL-138
 HMQC
 CDC13

01040806: Scan Avg 139-142 (27.70 - 28.30 min) - Back
Base: 279.00 Int: 2.02013e+006 Sample: VG 70-SE Positive Ion FAB

Sample: II-YL-138
Instrument Resolution: 7000
Theoretical Mass: (M+Na) 279.15722
Measured Mass: (M+Na) 279.15731
Error: 0.32 ppm

II-YL-140
PROTON
CDCl₃

II-YL-140
COSY
CDCl₃

II-YL-140
NOESY
CDCl₃

II-YL-140
CARBON
CDCl₃

II-YL-140
DEPT
CDCl₃

II-YL-140
HMQC
CDCl₃

01100806: Scan 35 (6.90 min) - Back
Base: 173.00 Int: 1.15405e+006 Sample: VG 70-SE Positive Ion FAB

Sample: II-YL-140
Instrument Resolution: 8000
Theoretical Mass: (M+Na) 275.12592
Measured Mass: (M+Na) 275.12622
Error: 1.09 ppm

II-YL-17
PROTON
C6D6

II-YL-17
COSY
C6D6

45

II-YL-17
NOESY
C6D6

II-YL-17
CARBON
C6D6

45

II-YL-17
DEPT
C6D6

45

II-YL-17
HMQC
C6D6

02011206: Scan Avg 66-69 (15.20 - 15.90 min) - Back
Base: 69.00 Int: 668532 Sample: VG70-SE Positive CI-Methane

Sample: II-YL-17

Instrument Resolution: 7000

Theoretical Mass: (M+H) 239.12833

Measured Mass: (M+H) 239.12747

Error: 3.60 ppm

II-YL-182
PROTON
CDCl₃

II-YL-182
COSY
CDCl₃

II-YL-182
NOESY
CDCl₃

II-YL-182
CARBON
CDCl₃

II-YL-182
DEPT
CDCl₃

27

II-YL-182
HMQC
CDCl₃

Y47 #52 RT: 4.83 AV: 1 NL: 2.47E6
T: + c Cl Full ms [69.50-800.50]

27

II-YL-174
PROTON
CDCl₃

II-YL-174
COSY
CDCl₃

II-YL-174
NOESY
CDCl₃

41

II-YL-174
CARBON
CDCl₃

41

II-YL-174
DEPT
CDCl₃

II-YL-174
HMQC
CDCl₃

01110806: Scan 66 (13.10 min) - Back
Base: 176.00 Int: 6.09178e+006 Sample: VG 70-SE Positive Ion FAB

Sample: II-YL-174
Instrument Resolution: 8000
Theoretical Mass: (M+Na) 279.12084
Measured Mass: (M+Na) 279.12075
Error: 0.32 ppm

II-YL-176
PROTON
CDCl₃

28

II-YL-176
COSY
CDCl₃

II-YL-176
NOESY
CDCl₃

II-YL-176
CARBON
CDCl₃

II-YL-176
DEPT
CDC13

191

II-YL-176
HMQC
CDCl₃

01040806: Scan Avg 154-155 (30.70 - 30.90 min) - Back
 Base: 393.00 Int: 3.24847e+006 Sample: VG 70-SE Positive Ion FAB

Sample: II-YL-176
 Instrument Resolution: 7000
 Theoretical Mass: (M+Na) 393.20731
 Measured Mass: (M+Na) 393.20688
 Error: 1.09 ppm

II-YL-155
PROTON
C6D6

29

II-YL-155
COSY
C6D6

29

II-YL-155
NOESY
C6D6

29

II-YL-155
DEPT
C6D6

II-YL-155
HMQC
C6D6

29

01110806: Scan Avg 80-81 (15.90 - 16.10 min) - Back
Base: 463.00 Int: 275383 Sample: VG 70-SE Positive Ion FAB

Sample: IL-YL-155
Instrument Resolution: 8000
Theoretical Mass: (M+Na) 463.24917
Measured Mass: (M+Na) 463.24980
Error: 1.36 ppm

II-YL-159
PROTON
C6D6

II-YL-159
COSY
C6D6

30

II-YL-159
NOESY
C6D6

II-YL-159
CARBON
C6D6

II-YL-159
DEPT
C6D6

II-YL-159
HMQC
C6D6

01110806: Scan Avg 12-13 (2:30 - 2:50 min) - Back
Base: 173.00 Int: 2.55476e+006 Sample: VG 70-SE Positive Ion FAB

II-YL-161
COSY
C6D6

31

II-YL-161
NOESY
C6D6

II-YL-161
CARBON
C6D6

31

II-YL-161
DEPT
C6D6

31

II-YL-161
HMQC
C6D6

01110806: Scan 109 (21.70 min) - Back
 Base: 377.00 Int: 1.00945e+006 Sample: VG 70-SE Positive Ion FAB

II-YL-151
PROTON
C6D6

II-YL-151
COSY
C6D6

II-YL-151
NOESY
C6D6

II-YL-151
CARBON
C6D6

II-YL-151
DEPT
C6D6

II-YL-151
HMQC
C6D6

01110806: Scan 165 (32.90 min) - Back
Base: 173.00 Int: 6.5535e+006 Sample: VG 70-SE Positive Ion FAB

Sample: II-YL-151

Instrument Resolution: 8000

Theoretical Mass: (M+Na) 293.13649

Measured Mass: (M+Na) 293.13724

Error: 2.56 ppm

6

III-YL-17a
PROTON
C6D6

III-YL-17a
COSY
C6D6

III-YL-17a
NOESY
C6D6

III-YL-17a
CARBON
C6D6

III-YL-17a
DEPT
C6D6

32

III-YL-17a
HMQC
C6D6

III-YL-17b
 PROTON
 C6D6

III-XL-17b
COSY
C6D6

III-YL-17b
NOESY
C6D6

III-YL-17b
CARBON
C6D6

III-YL-17b
DEPT
C6D6

33

III-YL-17b
HMQC
C6D6

III-YL-37b
 PROTON
 C6D6

III-YL-37b
COSY
C6D6

III-YL-37b
NOESY
C6D6

1

III-YL-37b
CARBON
C6D6

III-YL-37b
DEPT
C6D6

III-YL-37b
HMQC
C6D6

III-YL-26
PROTON
C6D6

III-YL-26
COSY
C6D6

35

III-YL-26
NOESY
C6D6

35

III-YL-26
CARBON
C6D6

III-YL-26
DEPT
C6D6

III-YL-26
HMQC
C6D6

01060906: Scan Avg 218-220 (43.50 - 43.90 min) - Back
Base: 173.00 Int: 649236 Sample: VG 70-SE Positive Ion FAB

Sample: III-YL-26
Instrument Resolution: 8000
Theoretical Mass: (M+Na) 413.19400
Measured Mass: (M+Na) 413.19337
Error: 1.52 ppm

III-YL-38
 PROTON
 CDCl₃

III-YL-38
COSY
CDCl₃

III-YL-38
NOESY
CDC13

4

III-YL-38
CARBON
CDCl₃

III-YL-38
DEPT
CDC13

III-YL-38
HMQC
CDCl₃

01021006: Scan Avg 104-108 (20.70 - 21.50 min) - Back
 Base: 154.00 Int: 1.16316e+006 Sample: VG 70-SE Positive Ion FAB

Sample: III-YL-30
 Instrument Resolution: 7000
 Theoretical Mass: (M+H) 363.18075
 Measured Mass: (M+H) 363.17937
 Error: 3.80 ppm

III-YL-39
 PROTON
 CDC13

(+)-Eremantholide A

III-YL-39
COSY
CDCl₃

(+)-Eremantholide A

III-YL-39
NOESY
CDC13

(+)-Eremantholide A

[illegible] [illegible]

III-YL-39
DEPT
CDC13

(+)-Eremantholide A

III-YL-39
HMQC
CDCl₃

(+)-Eremantholide A

III-YL-45
PROTON
CDCl₃

37

III-YL-45
COSY
CDCl₃

III-YL-45
NOESY
CDCl₃

III-YL-45
CARBON
CDCl₃

37

III-YL-45
DEPT
CDCl₃

37

III-YL-45
HMQC
CDCl₃

37

01061106: Scan Avg 165-166 (32.90 - 33.10 min) - Back
Base: 176.00 Int: 2.8361e+006 Sample: VG 70-SE Positive Ion FAB

Sample: III-YL-45
Instrument Resolution: 7000
Theoretical Mass (M+Na) 381.18891
Measured Mass: (M+Na) 381.18794
Error: 2.54 ppm

III-YL-45

III-YL-46
PROTON
CDCl₃

III-YL-46
NOESY
CDC13

III-YL-46
CARBON
CDCl₃

III-YL-46
DEPT
CDC13

III-YL-46
HMQC
CDCl₃

01061106: Scan Avg 152-153 (30.30 - 30.50 min) - Back
Base: 619.00 Int: 622256 Sample: VG 70-SE Positive Ion FAB

Sample: III-YL-46
Instrument Resolution: 7000
Theoretical Mass (M+Na) 619.30668
Measured Mass: (M+Na) 619.30708
Error: 0.66 ppm

III-YL-48
 PROTON
 CDCl₃

39

III-YL-48
COSY
CDCl₃

39

CDC13

III-YL-48
CARBON
CDCl₃

III-YL-48
DEPT
CDCl₃

III-YL-48
HMQC
CDCl₃

39

Asymmetric Total Synthesis and Formal Total Synthesis of the Antitumor Sesquiterpenoid (+)-Eremantholide A

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Supporting Information

Part 3. Individual 500 MHz ^1H NMR Spectra of 32 and 33 in CDCl_3 . The 500 MHz ^1H NMR Spectra of the Crude Unseparated Mixtures of 32 and 33 Obtained From the Alkylations of 2 with 3 Using Lithium bis[(*S*)-1- α -methylbenzylamide] and its (*R*)-Enantiomer in PhMe (-78 °C to 0 °C over 2 h). 400 MHz ^1H NMR Spectrum of 43 in CDCl_3 .

II-YL-72a
CDCl₃

32

II-YL-72b
CDCl₃

33

Alkylation of **2** with **3** in PhMe (-78 °C to 0 °C, over 2 h)
Mediated by Lithium Bis[(*S*)- α -methylbenzylamide]

II-YL-95 (crude mixture)
CDCl₃

II-YL-96 (crude mixture)
CDCl₃