Supporting Information:

Stereocontrolled [4+2]-Annulation Accessing Dihydropyrans: Synthesis of the C1a-C10 Fragment of Kendomycin

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General Information.

All reactions were carried out in oven or flame-dried glassware under an argon atmosphere employing standard techniques in handling air-sensitive materials. All solvents were reagent grade. Tetrahydrofuran (THF) was freshly distilled from sodium/benzophenone under argon immediately prior to use. Triethylamine, diisopropylethylamine, and 2,6-lutidine were distilled over calcium hydride and stored over potassium hydroxide. *n*-Butyllithium was purchased from Aldrich and standardized by titration with menthol/1,10-phenanthroline. Trimethylsilyl chloride was freshly distilled from quinoline before each use. Lithium bis(trimethylsilyl)amide solution was freshly prepared from 1,1,1,3,3,3-hexamethyldisilylazane and *n*-butyllithium before each use. All other reagents were used as supplied. Unless otherwise noted, reactions were magnetically stirred and monitored by thin layer chromatography with Sorbent Technologies 0.20 mm silica gel 60 plates. Flash chromatography were performed with silica gel 60 (particle size 0.032-0.063 mm) supplied by Sorbent Technologies. Yields refer to chromatographically and spectroscopically pure compounds, unless otherwise noted. ¹H NMR spectra were recorded using an internal deuterium lock at ambient temperature on a Varian 400 MHz spectrometer. An internal reference of δ_{H} 7.24 was used for CDCl₃. Data are presented as follows: chemical shift (in ppm on the δ scale relative to $\delta_{\text{TMS}} = 0$), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, quint. = quintuplet, m = multiplet, br = broad, ABq = AB quartet), coupling constant (*J*/Hz) and integration. Resonances that are either partially or fully obscured are denoted obscured (obsc). Carbon-13 NMR spectra were recorded on a Varian 75 MHz spectrometer. An internal reference of δ_{C} 77.16 was used for CDCl₃. Infrared spectra were recorded on a Nexus 670 FTIR spectrophotometer. Optical rotations were recorded on an Autopol III digital polarimeter at 589 nm and reported as follows: $[\alpha]_{\text{D}}^{20}$, concentration (*c* in g/100 mL) and solvent. High-resolution mass-spectra were obtained on a Finnigan MAT-90 spectrometer in the Boston University Mass Spectrometry Laboratory.

Experimental procedures:

(S)-Pent-3-yn-2-ol (4) and Acetic acid and (R)-1-methyl-but-2-ynyl ester (5): (18 g, 142.7 mmol) of racemic 1-methyl-but-2-ynyl ester^{1, 2} was placed into a round bottom flask with pH 7 buffer water (120 mL) followed by lipase Amano PS (18 g). The solution was rapidly stirred for 6 hours (Monitor by chiral GC).³ Extract solution with copious amounts of diethyl ether and dry over MgSO₄, filter and concentrate under vacuum⁴ to get a crude oil. Column over silica gel (gradient with hexanes/diethyl ether: 95/5; 90/10; 80/20) to get an ester (8.5 g, 47%) and an alcohol (4.0 g, 33%). Both compounds proved to be >98% ee.³

(S)-Pent-3-yn-2-ol (4): ¹H NMR (CDCl₃, 400 MHz): δ 4.7-4.1 (m, 1H), 2.40 (br s, 1H), 1.78 (d, J = 2.0 Hz, 3H), 1.38 (d, J = 6.4Hz, 3H); ¹³C NMR (75 MHz, CDCl₃): δ 81.6, 79.9, 58.2, 24.3, 3.6; IR (film) ν_{max} 3350, 2243cm⁻¹; HRMS(CI, NH₃) *m/z* calc'd for C₅H₈O [M+H]⁺ 84.1189, found: 84.0573; [α]_D²⁰ +27.3 (c 1.03, CHCl₃).⁵

(R)-1-methyl-but-2-ynyl ester (5): ¹H NMR (CDCl₃, 400 MHz): δ 5.33 (m, 1H), 1.99 (s, 3H), 1.76 (d, J = 1.8 Hz, 3H), 1.37 (d, J = 6.8 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃): δ 169.82, 80.89, 77.67, 60.67, 21.54, 20.96, 3.39; IR (film) ν_{max} 2264, 1737 cm⁻¹; HRMS(CI, NH₃) *m/z* calc'd for C₇H₁₀O₂ [M+H]⁺ 126.1566, found: ###.####; [α]_D²⁰ -7.8 (c 3.82, Et₂O).⁶

(1) Racemic 3-Pentyne-2-ol may be purchased from Fluka (77056) or prepared as described in: Gribble, G. W., Joyner, H. H., Switzer, F. L.; *Syn. Comm.* **1992**, 22, 2997.

(2) Preparation of 1-methyl-but-2-ynyl ester: Fleming, I.; Takaki, K.; Thomas, A. P. *J. Am. Chem. Soc. Perk. Trans. 1.* **1987**, 10, 2269.

(3) Chiraldex GC column at 80 °C isothermal gave: (R)-Pent-3-yn-2-ol at 11.05 min; : (S)-Pent-3-yn-2-ol at 11.61 min; (R)-1-methyl-but-2-ynyl ester at 14.71min; (S)-1-methyl-but-2-ynyl ester at 15.00 min.

(4) Both products are very volatile and will come off on rotoevaporation. Do not heat bath and monitor for evaporation to cease.

(5) Compares with: Ogawa, J.; Xie, S.; Shimizu, S. *Appl. Microbiol. Biotechnol.* **1999**, 51, 53.

(6) Compares with: Bach, R.; Brummel, R.; Holubka, J. *J. Org. Chem.* **1975**, 40, 2559.

(R)-Pent-3-yn-2-ol (6): (*R*)-1-methyl-but-2-ynyl ester **5** (8.00 g, 63.4 mmol) was added to a round bottom flask along with methanol (100 mL) and K_2CO_3 (1.8 g, 13 mmol). The reaction was rapidly stirred for 2 hours at ambient temperatures. Diethyl ether (500 mL) was then added followed by water (500 mL). The aqueous solution was then extracted twice more with diethyl ether and organics combined and washed with brine and dried over $MgSO_4$. The solution was filtered and then concentrated under vacuum to get a light yellow oil.⁴ Column over silica gel (hexanes/diethyl ether: 80/20) to get pure oil.

See above for spectroscopic data: $[\alpha]_D^{20}$ -25.1 (*c* 1.76, $CHCl_3$).

(E)-4-(Dimethyl-phenyl-silanyl)-pent-3-en-2-ol (7): Racemic 3-pentyn-2-ol⁷ (10 g, 118.9 mmol) was dissolved in THF (360 mL) was cooled to 0 °C. In a separate flask a 1M solution of lithium dimethylphenylsilane⁸ in THF (238 mL, 238 mmol) was slowly added to a 1M solution of diethyl zinc in pentane (238 mL, 238 mmol) at 0 °C. This solution was allowed to stir for 15 minutes at which time copper cyanide (500 mg, 5 mol %) was added followed by the addition of the alcohol/THF solution via cannula at 0 °C for 15 minutes. After addition is complete the solution is allowed to warm to ambient temperature and stir here for an additional hour. The entire solution is then carefully poured into a saturated solution of NH_4Cl and the aqueous layer extracted with diethyl ether. The combined organic layers were then dried over $MgSO_4$, filtered over silica gel and concentrated under vacuum to give a yellow oil. Column over silica gel (hexanes/ethyl acetate: 80/20) to get a semi pure oil.⁹ Further purification of vinyl silane may be achieved through distillation to give a clear oil.¹⁰ 1H NMR ($CDCl_3$, 400 MHz): δ 7.47 (m, 2H), 7.33 (m, 3H), 5.80 (dq, J = 7.6 Hz, 1.6Hz, 1H), 4.74 (quint, J = 6.4 Hz, 1H), 1.69 (s, 3H), 1.23 (dd, J = 6.4 Hz, 1.2 Hz, 3H), .33 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): 144.7, 137.9, 135.2, 133.9, 128.9, 127.7, 64.2, 22.8, 14.7, -3.9, -3.9; IR (film) ν_{max} 3331, 2964, 1427, 1248, 814 cm^{-1} ; HRMS(CI, NH_3) m/z calc'd for $C_{13}H_{20}OSi$ $[M+H]^+$ 220.3867, found: 220.1349.

(7) The reaction may also be carried out on optically pure alcohol **6**.

(8) Trost, B. M., Tour, J. M. *J. Org. Chem.* **1998**, 54, 484.

(9) $PhMe_2Si-SiMe_2Ph$, one of the by-products of this reaction is very difficult to separate via column.

(10) If impurity in reference 9 is not removed the resolution is very sluggish.

Acetic acid (*E*)-(*R*)-3-(dimethyl-phenyl-silanyl)-1-methyl-but-2-enyl ester (7c) and (*E*)-(*S*)-4-(Dimethyl-phenyl-silanyl)-pent-3-en-2-ol (7d): Racemic alcohol **7** (6.48 g, 29.46 mmol) was dissolved up in hexane (120 mL) and rapidly stirred while (6.48 g) Amano AK lipase was added. The flask is then sealed and vinyl acetate (9.41 mL, 147.3 mmol) was added. The resulting suspension was allowed to stir for approximately 52 hours. Once deemed complete via NMR the solution was filter and concentrated under vacuum to get a yellow oil. The resulting oil can be purified using a gradient elution with (hexane/ethyl acetate: 98/2; 95/5; 90/10; 80/20) to first get an acetate (3.15 g, 90%) followed by (3.10 g, 96%) of an alcohol.

Acetic acid (*E*)-(*R*)-3-(dimethyl-phenyl-silanyl)-1-methyl-but-2-enyl ester (7c): ^1H NMR (CDCl_3 , 400 MHz): δ 7.48-7.43 (m, 2H), 7.35-7.30 (m, 3H), 5.75-5.67 (obsc. quint, $J = 6.0$ Hz, 1H), 5.73 (obsc. quint, $J = 1.6$ Hz, 1H), 2.02 (s, 3H), 1.71 (d, $J = 1.6$ Hz, 1H), 1.25 (d, $J = 6.0$ Hz, 3H), .33 (s, 6H); ^{13}C NMR (75 MHz, CDCl_3): 170.3, 139.9, 137.6, 137.4, 133.9, 129.0, 127.8, 67.5, 21.1, 20.1, 14.9, -3.8, -3.9; IR (film) ν_{max} 2958, 1738, 1369, 1242, 1042, 833 cm^{-1} ; HRMS(CI, NH_3) m/z calc'd for $\text{C}_{15}\text{H}_{22}\text{O}_2\text{Si}$ $[\text{M}+\text{H}]^+$ 262.4239, found: 262.1396; $[\alpha]_{\text{D}}^{20} +5.07$ (c 1.11, CHCl_3).

(*E*)-(*S*)-4-(Dimethyl-phenyl-silanyl)-pent-3-en-2-ol (7d): ^1H , ^{13}C , IR and HRMS were identical to that of compound. $[\alpha]_{\text{D}}^{20} -24.6$ (c 1.31, CHCl_3).¹¹

(*E*)-(*R*)-4-(Dimethyl-phenyl-silanyl)-pent-3-en-2-ol (7a): Acetic acid (*E*)-(*R*)-3-(dimethyl-phenyl-silanyl)-1-methyl-but-2-enyl ester **7c** (2.8 g, 11.72 mmol) is dissolved in diethyl ether (40 mL) under a nitrogen atmosphere and cooled to 0°C. To this solution LiAlH_4 (.61 g, 15.23 mmol) was slowly added. After approximately 1 hour, slow addition of 5% HCl commenced until bubbling ceases. The resulting suspension is further diluted and the aqueous layer extracted with diethyl ether. The combined extracts are dried over MgSO_4 , filtered and concentrated under vacuum to get a crude yellow oil. A silica plug (hexane/ethyl: 80/20) was then run to get a light yellow/clear oil (2.3 g, 89%). ^1H , ^{13}C , IR and HRMS were identical to that of racemic compound. $[\alpha]_{\text{D}}^{20} + 20.1$ (c 1.22, CHCl_3).¹²

(11) The ee of this product was determined to be 92 % by chiral HPLC analysis (Chiracel OD, hexanes/*i*PrOH: 99/1, 1 mL.min⁻¹, t_{R} (minor) 12.3 min, t_{R} (major) 17.6 min).

(12) The ee of this product was determined to be 99 % by chiral HPLC analysis (Chiracel OD, hexanes/*i*PrOH: 99/1, 1 mL.min⁻¹, t_{R} (minor) 12.3 min, t_{R} (major) 17.6 min).

Injection Date : 10/21/03 8:47:36 AM

Sample Name : racemic

Acq. Operator : jason

Location : Vial 1

Inj Volume : 10 µl

Method : C:\HPCHEM\1\METHODS\XL.M

Last changed : 10/21/03 8:42:25 AM by jason
(modified after loading)

Area Percent Report

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Sample Amount : 5.00000 [ng/ul] (not used in calc.)

Signal 1: MWD1 A, Sig=250,100 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.778	MM	0.7243	1.05076e4	241.80145	50.3267
2	17.619	MM	0.8387	1.03712e4	206.09099	49.6733

Totals : 2.08788e4 447.89244

Results obtained with enhanced integrator!

Signal 2: MWD1 B, Sig=254,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.777	MM	0.6951	427.18231	10.24322	49.4224
2	17.615	MM	0.8260	437.16733	8.82064	50.5776

Totals : 864.34964 19.06386

Instrument 1 10/21/03 9:21:50 AM jason

File C:\HPCHEM\1\DATA\JL\RACEMIC.D

Results obtained with enhanced integrator!

Signal 3: MWD1 C, Sig=210,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.778	MM	0.6725	3.87563e4	960.55182	49.0022
2	17.619	MM	0.8159	4.03345e4	823.91534	50.9978

Totals : 7.90908e4 1784.46716

Results obtained with enhanced integrator!

Signal 4: MWD1 D, Sig=230,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.778	MM	0.7321	9232.93457	210.18961	52.2284
2	17.622	MM	0.8112	8445.06152	173.50830	47.7716

Totals : 1.76780e4 383.69791

Results obtained with enhanced integrator!

Signal 5: MWD1 E, Sig=280,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.782	MM	0.4934	31.21510	1.05448	43.1065
2	17.610	MM	0.6760	41.19888	1.01582	56.8935

Injection Date : 10/21/03 9:24:48 AM
Sample Name : acetate/alcohol
Acq. Operator : jason

Location : Vial 2

Inj Volume : 10 µl

Method : C:\HPCHEM\1\METHODS\XL.M
Last changed : 10/21/03 8:42:25 AM by jason
(modified after loading)

Area Percent Report

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Sample Amount : 5.00000 [ng/ul] (not used in calc.)

Signal 1: MWD1 A, Sig=250,100 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.305	MM	0.7186	1.71523e4	397.81146	95.3868
2	17.078	MM	0.6935	829.53259	19.93607	4.6132

Totals : 1.79819e4 417.74754

Results obtained with enhanced integrator!

Signal 2: MWD1 B, Sig=254,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.305	MM	0.6776	760.89313	18.71428	93.7951
2	17.080	MM	0.8151	50.33628	1.02921	6.2049

Totals : 811.22941 19.74348

Instrument 1 10/21/03 10:11:56 AM jason

File C:\HPCHEM\1\DATA\JL\ACET-ALC.D

Results obtained with enhanced integrator!

Signal 3: MWD1 C, Sig=210,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.305	MM	0.7082	7.20940e4	1696.53076	94.4204
2	17.081	MM	0.7389	4260.23975	96.10011	5.5796

Totals : 7.63542e4 1792.63087

Results obtained with enhanced integrator!

Signal 4: MWD1 D, Sig=230,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.305	MM	0.7094	1.58633e4	372.70468	95.9301
2	17.069	MM	0.6781	673.00873	16.54188	4.0699

Totals : 1.65363e4 389.24656

Results obtained with enhanced integrator!

Signal 5: MWD1 E, Sig=280,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.306	MM	0.7905	119.30357	2.51527	86.5450
2	17.057	MM	0.3853	18.54786	6.28457e-1	13.4550

1%IPA in Hexane
1.0 ml/min
chiracel OD (Porco)

Injection Date : 10/23/03 11:33:37 AM

Sample Name : 2ndres

Acq. Operator : yz

Location : Vial 1

Inj Volume : 10 µl

Method : C:\HPCHEM\1\METHODS\WLT.M

Last changed : 10/23/03 11:25:17 AM by yz

(modified after loading)

Area Percent Report

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Sample Amount : 10.00000 [ng/ul] (not used in calc.)

Signal 1: MWD1 A, Sig=250,100 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.846	VB	0.5288	887.77545	24.26641	6.7213
2	17.532	BB	0.7378	1.23206e4	243.72893	93.2787

Totals : 1.32084e4 267.99534

Results obtained with enhanced integrator!

Signal 2: MWD1 B, Sig=254,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.849	MM	0.5008	27.09018	9.01571e-1	5.8342
2	17.532	BB	0.6381	437.24664	10.15972	94.1658

Totals : 464.33683 11.06129

Results obtained with enhanced integrator!

Signal 3: MWD1 C, Sig=210,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.845	VB	0.5630	3766.49414	95.73358	7.1126
2	17.532	PB	0.7279	4.91887e4	982.82458	92.8874

Totals : 5.29552e4 1078.55817

Results obtained with enhanced integrator!

Signal 4: MWD1 D, Sig=230,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.248	BV	0.4648	91.27124	2.78200	0.8096

Determination of absolute stereochemistry of (*E*)-4-(Dimethyl-phenyl-silanyl)-pent-3-en-2-ol.

The absolute stereochemistry of the chiral vinyl silanes were assigned by Mosher analysis after the conversion of each of the above alcohols to an (*R*)-mandelate ester. Comparison of ^1H NMR spectra of each derived mandelate ester established the absolute configuration at the carbinol center.

(*R*)-Acetoxy-phenyl-acetic acid (*E*)-(S)-3-(dimethyl-phenyl-silanyl)-1-methyl-but-2-enyl ester (7e): (*E*)-(S)-4-(Dimethyl-phenyl-silanyl)-pent-3-en-2-ol **7d** (.05 g, .255 mmol) was added into a round bottom flask along with DCC .071g (.071g, .344 mmol), DMAP (.003 g, .0255 mmol) and CH_2Cl_2 (1 mL). A solution of (*R*)-acetoxymandelic acid (.05 g, .255mmol) in CH_2Cl_2 (1mL) was then added at room temperature. The reaction was allowed to stir overnight at room temperature. The solution was filter and concentrated under vacuum to get a cloudy oil. The oil was then purified over silica gel (hexanes/ethyl acetate: 98/2) to get a clear oil (.074 g, 75%). ^1H NMR (CDCl_3 , 400 MHz): δ 7.43 (m, 4H), 7.33 (m, 6H), 5.88 (s, 1H), 5.72 (m, 2H), 2.17 (s, 3H), 1.67 (d, J = .8 Hz, 3H), 1.14 (d, J = 6.4 Hz, 3H), .313 (s, 6H); ^{13}C NMR (75 MHz, CDCl_3): δ 170.1, 168.0, 138.8, 138.7, 137.5, 134.0, 133.9, 129.0, 129.0, 128.6, 127.7, 127.5, 74.6, 69.1, 20.7, 19.8, 15.2, -3.7; IR (film) ν_{max} 2956, 1746, 1372, 1232 cm^{-1} ; HRMS(CI, NH_3) m/z calc'd for $\text{C}_{22}\text{H}_{28}\text{O}_3\text{Si}$ $[\text{M}+\text{H}]^+$ 396.5584, found: 396.1759; $[\alpha]_{\text{D}}^{20}$ -57.0 (c 1.10, CHCl_3).

(*R*)-Acetoxy-phenyl-acetic acid (*E*)-(R)-3-(dimethyl-phenyl-silanyl)-1-methyl-but-2-enyl ester (7f): **7a** (.05 g, .255 mmol) was added into a round bottom flask along with .071g DCC (.071 g, .344 mmol), DMAP (.003 g, .0255 mmol) and CH_2Cl_2 (1 mL). A solution of (*R*)-acetoxymandelic acid (.05 g, .255 mmol) in CH_2Cl_2 (1 mL) was then added at room temperature. The reaction was allowed to stir overnight at room temperature. The solution was filter and rotoevaporated to get a cloudy oil. The oil was then purified over silica gel (hexanes/ethyl acetate: 98/2) to get a clear oil (.074 g, 75%). ^1H NMR (CDCl_3 , 400 MHz): δ 7.40 (m, 2H), 7.33 (m, 8H), 5.86 (s, 1H), 5.70 (q, J = 8.4Hz, 1H), 5.43 (app. dq, J = 10.4 Hz, 2.0 Hz, 1H), 2.16 (s, 3H), 1.57 (d, J = 2 Hz, 3H), 1.28 (d, J = 8.4 Hz, 3H), .210 (s, 6H); ^{13}C NMR (75 MHz, CDCl_3): δ 170.4, 168.2, 139.2, 138.7, 137.5, 134.1, 133.9, 129.1, 129.0, 128.7, 127.8, 127.7, 74.6, 68.8, 20.6, 19.8, 14.9, -3.9, -4.0; IR (film) ν_{max} 2957, 1746, 1372, 1232 cm^{-1} ; HRMS(CI, NH_3) m/z calc'd for $\text{C}_{22}\text{H}_{28}\text{O}_3\text{Si}$ $[\text{M}+\text{H}]^+$ 396.5634, found: 396.1803; $[\alpha]_{\text{D}}^{20}$ +32.0 (c 1.04, CHCl_3).

(E)-(R)-3-(Dimethyl-phenyl-silanyl)-3-methyl-hex-4-enoic acid methyl ester (7g): A solution of **7a** (1.83 g, 9.34 mmol) in toluene (20 mL) was added trimethyl orthoacetate (4.75 mL, 37.3mmol) and propionic acid (.037 mL, .47mmol). The solution is then heated to reflux and stirred for 48 hours. Solution is then cooled and concentrated under reduced pressure to leave a yellow oil. The crude oil is purified over silica gel (hexane/ethyl acetate: 98/2) to afford of a faint yellow oil (1.9 g, 79%). ¹H NMR (CDCl₃, 400 MHz): δ 7.46-7.42 (m, 2H), 7.36-7.28 (m, 3H), 5.44 (dq, J= 15.2 Hz, 1.6 Hz, 1H), 5.09 (dq, J= 15.2 Hz, 6.4 Hz, 1H), 3.53 (s, 3H), 2.38 (d, J_{ab}= 13.6 Hz, 1H), 2.20 (d, J_{ab}= 13.2 Hz, 1H), 1.67 (dd, 6.4 Hz, 3H), 1.10 (s, 3H), .26 (s, 6H); ¹³C NMR (75 MHz, CDCl₃): δ 172.6, 136.1, 135.3, 134.7, 129.2, 127.5, 121.7, 50.8, 40.8, 28.4, 18.2, -6.3, -6.4; IR (film) ν_{max} 2956, 1736, 1428, 1249, 1215, 1114, 832 cm⁻¹; HRMS(CI, NH₃) *m/z* calc'd for C₁₆H₂₄O₂Si [M+H]⁺ 267.4508, found: 276.1553; [α]_D²⁰ -14.8 (c 1.27, CHCl₃).

(E)-(S)-3-(Dimethyl-phenyl-silanyl)-3-methyl-hex-4-enoic acid methyl ester (ent-7g): [α]_D²⁰ +14.4 (c 1.21, CHCl₃).

(4-Methoxy-benzyloxy)-acetic acid (E)-(S)-3-(dimethyl-phenyl-silanyl)-1-methyl-but-2-enyl ester (8a): **7a** (1.70 g, 7.73 mmol) was placed in a round bottom flask and dissolved in CH₂Cl₂ (25 mL) and cooled to 0 °C. DCC (2.15 g, 10.4 mmol) and DMAP (.094 g, 10mol%) was added followed by slow addition of PMB acid¹³ (1.5 g, 7.73 mmol) dissolved in CH₂Cl₂ (4 mL) over 15min followed by a CH₂Cl₂ (0.5 mL) rinse. Allow solution to warm to room temperature over night in ice bath. White precipitate is then filtered off and solution concentrated under vacuum. Cloudy yellow/orange oil is then purified using a gradient elution on silica gel (hexanes/ethyl acetate: 98/2; 95/5; 90/10) to give of light yellow to clear oil (2.84 g, 92%). ¹H NMR (CDCl₃, 400 MHz): δ 7.45 (m, 2H), 7.32 (m,3H), 7.27 (d, J = 8.8 Hz, 2H), 6.86 (d, J = 8.8 Hz, 2H), 5.80 (quint, J = 6.4 Hz, 1H), 5.72 (dq, J= 6.4 Hz, 1.6 Hz, 1H), 4.54 (s, 2H), 4.02 (s, 2H), 3.79 (s, 3H), 1.73 (d, J= 1.6 Hz, 3H), 1.28 (d, J= 2.4 Hz, 3H), .32 (s, 6H); ¹³C NMR (75 MHz, CDCl₃): δ 169.8, 159.5, 139.3, 138.2, 137.6, 134.0, 129.8, 129.2, 129.1, 127.8, 113.8, 72.8, 68.1, 66.9, 55.1, 20.2, 15.1, -3.8, -3.9; IR (film) ν_{max} 2955, 1750, 1613, 1514, 1249, 1112, 1037, 815 cm⁻¹; HRMS(CI, NH₃) *m/z* calc'd for C₂₂H₂₈O₃Si [M+H]⁺ 368.5490, found: 368.1838; [α]_D²⁰ +20.2 (c 1.08, CHCl₃).

¹³ Abraham, D.; Kennedy, P.; Mehanna, A.; Patwa, D.; Williams. F. J. *Med. Chem.* **1984**, 27, 967.

(4-Methoxy-benzyloxy)-acetic acid (*E*)-(*R*)-3-(dimethyl-phenyl-silanyl)-1-methyl-but-2-enyl ester (ent-8a): $[\alpha]_{\text{D}}^{20}$ -20.8 (*c* 1.18, CHCl₃).

(*E*)-(2*S*,3*S*)-3-(Dimethyl-phenyl-silanyl)-2-(4-methoxy-benzyloxy)-3-methyl-hex-4-enoic acid (9a): Anhydrous THF (60 mL) and HMDS (1.95 mL, 9.28 mmol) were added to a 250 mL round bottom flask and cooled to 0 °C. Slow addition of 2.5M *n*-butyl lithium solution in hexanes (3.7 mL, 9.28 mmol) then commenced after which the light yellow solution was stirred for 15 minutes before being brought to -78 °C and allowed to stir for an additional 15 minutes. In a separate 100mL round bottom flask was added **8a** (2.84 g, 7.14 mmol) which, was subsequently dissolved in THF (60 mL) and cooled to -78 °C. The flask containing the silane was cannulated to the base solution over approximately a 30 minute period. The solution was then allowed to stir for an additional 1 hour at -78 °C. To the bright yellow solution was added TMSCl (2.63 mL, 21.4 mmol) over 15 minutes. The clear (sometimes cloudy white) solution is then allowed to warm to ambient temperature on its own overnight. At this point a saturated solution of NH₄Cl was added followed by extraction with diethyl ether. The combined organic layers were then dried over MgSO₄, filtered and the solvent evaporated under vacuum to give a light yellow oil. Purification by flash chromatography on silica gel (hexanes/ethyl acetate: 90/10) gives an acid (2.48 g, 87%) as a clear oil which, solidifies (white solid) on standing. ¹H NMR (CDCl₃, 400 MHz): δ 7.40 (dd, *J* = 6.4 Hz, 1.2 Hz, 2H), 7.31 (m, 4H), 7.23 (d, 1H), 6.87 (d, *J* = 8.8 Hz, 2H), 5.46 (dd, *J* = 16 Hz, 1.6 Hz, 1H), 5.08 (dq, *J* = 16 Hz, 6.4 Hz, 1H), 4.36 (d, *J*_{ab} = 10.8 Hz, 1H), 4.12 (d, *J*_{ab} = 10.8 Hz, 1H), 3.82 (s, 1H), 3.81 (s, 3H), 1.65 (dd, *J* = 6.4 Hz, 1.2 Hz, 3H), 1.11 (s, 3H), .26 (s, 3H), .19 (s, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 176.7, 159.4, 136.9, 134.8, 132.4, 129.9, 129.3, 129.1, 127.3, 122.4, 113.7, 82.9, 71.9, 55.1, 35.5, 18.2, 14.0, -4.1, -4.1; IR (film) ν_{max} 2955, 1712, 1613, 1514, 1249, 1110, 820 cm⁻¹; HRMS(CI, NH₃) *m/z* calc'd for C₂₃H₃₀O₄Si [M+H]⁺ 398.574, found: 398.569; $[\alpha]_{\text{D}}^{20}$ +16.4 (*c* 1.38, CHCl₃).

(*E*)-(2*R*,3*R*)-3-(Dimethyl-phenyl-silanyl)-2-(4-methoxy-benzyloxy)-3-methyl-hex-4-enoic acid (ent-9a): $[\alpha]_{\text{D}}^{20}$ -14.2 (*c* 1.09, CHCl₃).

(*E*)-(2*S*,3*S*)-3-(Dimethyl-phenyl-silanyl)-2-(4-methoxy-benzyloxy)-3-methyl-hex-4-enoic acid methyl ester (9c): To a flask with **9a** (3.28 g, 8.3 mmol) was added a saturated NaHCO₃ solution (28 mL). To a second flask is added adogen-464 (3.36 g, 8.3mmol) followed by CH₂Cl₂ (28 mL) and iodomethane (0.62 mL, 9.97 mmol). The

second solution containing the adogen/MeI mix is poured into the initial flask in one shot at room temperature followed by a CH₂Cl₂ rinse (2 mL). The heterogeneous mixture is then rapidly stirred at room temperature overnight. The mixture is then diluted with water and extracted with CH₂Cl₂. The extracts are then dried over MgSO₄, filtered and concentration under vacuum to obtain a light yellow oil. The oil may be purified via flash chromatography over silica gel using a gradient elution (hexanes/ethyl acetate: 95/5; 90/10) to obtain a clear oil (3.1 g, 92%). ¹H NMR (CDCl₃, 400 MHz): δ 7.38 (d, 2H), 7.27 (m, 5H), 6.87 (d, 2H), 5.43 (dd, J = 15.6 Hz, 1.2 Hz, 1H), 5.04 (dq, J = 15.6 Hz, 6.4 Hz, 1H), 4.35 (d, J_{ab} = 10.8 Hz, 1H), 4.05 (d, J_{ab} = 10.8 Hz, 1H), 3.82 (s, obsc, 1H), 3.81 (s, 3H), 3.57 (s, 3H), 1.63 (dd, J = 6.4 Hz, 1.2 Hz, 3H), 1.10 (s, 3H), .24 (s, 3H), .17 (s, 3H); ¹³C NMR (75 MHz, CDCl₃) 171.5, 159.3, 137.0, 134.8, 132.7, 129.9, 129.5, 128.9, 127.3, 121.9, 113.6, 83.0, 71.6, 55.1, 50.6, 35.5, 18.1, 13.9, -4.1, -4.2; IR (film) ν_{max} 3019, 2954, 1737, 1514, 1215, 757 cm⁻¹; HRMS(CI, NH₃) *m/z* calc'd for C₂₄H₃₂O₄Si [M+H]⁺ 412.574, found: 412.500; [α]_D²⁰ +15.4 (*c* 1.38, CHCl₃).

(*E*)-(2*R*,3*R*)-3-(Dimethyl-phenyl-silanyl)-2-(4-methoxy-benzyloxy)-3-methyl-hex-4-enoic acid methyl ester (ent-9c): [α]_D²⁰ -14.7 (*c* 1.46, CHCl₃).

(*E*)-(2*S*,3*S*)-3-(Dimethyl-phenyl-silanyl)-2-hydroxy-3-methyl-hex-4-enoic acid methyl ester (9d): 9c (2.76 g, 6.75 mmol) was placed in a round bottom flask with CH₂Cl₂ (168 mL) and of H₂O (16.8 mL, 10% by volume) and was cooled to 0 °C. The solution was rapidly stirred while DDQ (3.12 g, 13.5 mmol) was added. Once addition was complete the red/brown solution was stirred at 0 °C for 2 hours then warmed to room temperature and stirred overnight. A saturated solution of NaHCO₃ was added and aqueous layer extracted with CH₂Cl₂ combined with previous organic layer and extracted 2 more times with sat NaHCO₃ solution followed by a brine extraction. Organic layers are then dried over MgSO₄, filtered and concentrated under vacuum to get a orange/brown oil. Purification of the resulting oil over silica gel using a gradient elution (hexanes/ethyl acetate: 99/1; 98/2) resulted in a clear oil. ¹H NMR (CDCl₃, 400 MHz): δ 7.54 (m, 2H), 7.33 (m, 3H), 5.42 (dd, J = 16 Hz, 1.6 Hz, 1H), 5.04 (dq, J = 16 Hz, 6.4 Hz, 1H), 4.09 (s, 1H), 3.59 (s, 3H), 2.75 (broad s, 1H), 1.65 (dd, J = 6.4 Hz, 1.6 Hz, 3H), .96 (s, 3H), .36 (s, 3H), .26 (s, 3H); ¹³C NMR (75 MHz, CDCl₃) 174.5, 136.9, 134.8, 132.8, 128.9, 127.3, 121.7, 75.6, 51.3, 36.6, 18.1, 13.3, -3.8, -4.6; IR (film) ν_{max}: 3505, 2953, 1727, 1254, 972 cm⁻¹; HRMS(CI, NH₃) *m/z* calc'd for C₁₆H₂₄O₃Si [M+H]⁺ 292.450, found: 292.152; [α]_D²⁰ -58.4 (*c* 1.25, CHCl₃).

(*E*)-(2*R*,3*R*)-3-(Dimethyl-phenyl-silanyl)-2-hydroxy-3-methyl-hex-4-enoic acid methyl ester (ent-9d): [α]_D²⁰ +59.0 (*c* 1.44, CHCl₃).

(E)-(2S,3S)-3-(Dimethyl-phenyl-silanyl)-3-methyl-2-trimethylsilanyloxy-hex-4-enoic acid methyl ester (4a): α -hydroxysilane **9d** (1.58 g, 5.39 mmol) in CH_2Cl_2 (18 mL) was cooled to 0 °C and 2,6-lutidine (1.19 mL, 10.8 mmol) was added. Slow addition of 99% TMSOTf (1.06 mL, 5.71 mmol) then commenced over 15 minutes. The mixture is stirred at 0 °C for 2 hours after which water is added and extracted with CH_2Cl_2 . The combined organic layers are then dried over MgSO_4 , filtered and concentrated under vacuum to get a clear oil. The oil was then purified over silica gel (hexane/ethyl acetate: 98/2) to get a clear oil (1.91 g, 97%). ^1H NMR (CDCl_3 , 400 MHz): δ 7.45 (m, 2H), 7.31 (m, 3H), 5.44 (dd, J = 15.6 Hz, 1.6 Hz, 1H), 4.95 (dq, J = 15.6 Hz, 6.4 Hz, 1H), 4.20 (s, 1H), 3.53 (s, 3H), 1.60 (dd, J = 6.4 Hz, 1.6 Hz, 3H), 1.06 (s, 3H), .33 (s, 3H), .25 (s, 3H), .047 (s, 9H); ^{13}C NMR (75 MHz, CDCl_3): 174.4, 137.3, 134.9, 132.6, 128.9, 127.2, 122.2, 76.9, 50.5, 36.4, 18.1, 13.5, .22, -.18, -4.0, -4.4; IR (film) ν_{max} 2954, 1749, 1252, 1113, 842 cm^{-1} ; HRMS(CI, NH_3) m/z calc'd for $\text{C}_{19}\text{H}_{32}\text{O}_3\text{Si}_2$ $[\text{M}+\text{H}]^+$ 364.632, found: 364.187; $[\alpha]_{\text{D}}^{20}$ -18.2 (c 1.06, CHCl_3).

(E)-(2R,3R)-3-(Dimethyl-phenyl-silanyl)-3-methyl-2-trimethylsilanyloxy-hex-4-enoic acid methyl ester (ent-4a): $[\alpha]_{\text{D}}^{20}$ +18.5 (c 1.21, CHCl_3).

(Z)-(R)-4-Iodo-pent-3-en-2-ol (6a): Red-Al[®] (11.6 mL, 38.6 mmol) was added to a round bottom flask under nitrogen followed by diethyl ether (60 mL). The reaction flask was cooled to 0 °C and a solution 3-Pentyn-2-ol **6** (1.50 g, 17.8 mmol) in diethyl ether (10 mL) was added dropwise. Allow to warm to room temperature and stir for an additional 4 hours. Re-cool mixture to 0 °C and quench with ethyl acetate (1.86 mL, 19mmol). Bring the solution to -78 °C and add iodine (7.24 g, 28.5 mmol) in one shot. Allow solution to warm to room temperature slowly overnight in dry ice bath. The reaction mixture was quenched by slow addition of Na_2SO_3 , and the organic layer separated and washed with Na_2SO_3 , water and brine. The resulting solution was dried over MgSO_4 , filtered and concentrated to get a light yellow oil. Column over silica gel with a gradient elution (hexanes/ethyl acetate: 95/5; 90/10; 80/20) to get an light yellow oil (3.10g, 82%). (May be taken to next step crude) ^1H NMR (CDCl_3 , 400 MHz): δ 5.54-5.51 (dq, J = 7.6 Hz, 1.2 Hz, 1H), 4.39 (q, J = 6.8 Hz, 1H), 2.49 (dd, J = 7.6 Hz, 1.2 Hz, 1H), 4.38-4.31 (quint, J = 7.2 Hz, 1H), 2.4 (d, J = 1.2Hz), 1.71 (brs, 1H), 1.26 (d, J = 6.4 Hz, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ ; 138.76, 99.72, 72.69, 33.46, 21.86; IR (film) ν_{max} 3335, 2971, 1649, 1108, 1066 cm^{-1} ; HRMS(CI, NH_3) m/z calc'd for $\text{C}_5\text{H}_9\text{IO}$ $[\text{M}+\text{H}]^+$ 212.0313, found: 211.9674; $[\alpha]_{\text{D}}^{20}$ +3.5 (c 2.40, CHCl_3).

(Z)-(R)-3-Iodo-1-methyl-but-2-enyloxy)-dimethyl-phenyl-silane (6b): Vinyl iodide **6a** (5g, 23.6 mmol) was dissolved in CH_2Cl_2 (120 mL) and cooled to 0 °C. DMAP (0.028 g, 0.236 mmol) and triethyl amine (3.44 mL, 24.8 mmol) was then added. At 0 °C chlorodimethylphenylsilane (4.00 mL, 23.6 mmol) was added dropwise over 30 minutes and the reaction mixture stirred for 1 hour at 0 °C then 1 hour at room temperature before being poured into a saturated solution of NH_4Cl . The organic layer was separated and dried over MgSO_4 , filtered and concentrated under vacuum. This oil was re-dissolved in pentane and washed with water and brine. Dry organics over MgSO_4 , filter and concentrated to get a yellow oil. Column over silica gel with a gradient elution (hexanes/ethyl acetate: 98:2; 95:5; 90:10) to get a light yellow oil (7.20 g, 88%). (May be taken to next step crude) ^1H NMR (CDCl_3 , 400 MHz): δ 7.58-7.55 (m, 2H), 7.37-7.33 (m, 3H), 5.46-5.44 (dd, $J = 7.6$ Hz, 1.2 Hz, 1H), 4.38-4.31 (quint, $J = 7.2$ Hz, 1H), 2.4 (d, $J = 1.2$ Hz), 1.16-1.15 (d, 6.4 Hz, 3H), .386-.378 (d, 6H); ^{13}C NMR (75 MHz, CDCl_3) δ ; 139.40, 137.99, 133.54, 129.53, 127.76, 98.07, 74.42, 33.35, 22.96, -1.51, -1.27; IR (film) ν_{max} 2969, 1649, 1427, 1252, 1117, 827 cm^{-1} HRMS(CI, NH_3) m/z calc'd for $\text{C}_{19}\text{H}_{19}\text{OSi}$ $[\text{M}+\text{H}]^+$ 346.2801, found: 346.0285; $[\alpha]_{\text{D}}^{20} +51.3$ (c 1.06, CHCl_3).

(Z)-(R)-4-(Dimethyl-phenyl-silanyl)-pent-3-en-2-ol¹⁴ 7b: DMPSi protected vinyl iodide **6b** (7.0 g, 20.2 mmol) was dissolved in THF (120 mL) and cooled to -78 °C under nitrogen. $t\text{-BuLi}$ (26 mL, 44 mmol) was then added dropwise over a period of 10 minutes and stirred for 2 hours at the same temperature. A saturated solution of NH_4Cl was then added to the flask and allowed to warm to room temperature. The aqueous layer was extracted with diethyl ether and combine organics dried over MgSO_4 . Filter off drying agent and concentrated to get a yellow oil. Column over silica gel with a gradient (hexanes/ethyl acetate: 95:5; 90:10; 80:20) to get a light yellow oil (4.00 g, 90%). ^1H NMR (CDCl_3 , 400 MHz): δ 7.51-7.45 (m, 2H), 7.35-7.33 (m, 3H), 6.04-6.00 (dq, $J = 7.6$ Hz, 1.6 1H), 4.30-4.23 (m, 1H), 1.83 (d, $J = 2.0$ Hz, 3H), 1.06 (d, $J = 6.4$ Hz, 3H), .39 (s, 6H); ^{13}C NMR (75 MHz, CDCl_3) δ 147.0, 139.2, 135.4, 133.5, 129.1, 128.0, 67.0, 24.8, 22.7, -1.36, -1.45; IR (film) ν_{max} 3346, 2967, 1620, 1428 1050 cm^{-1} ; HRMS(CI, NH_3) m/z calc'd for $\text{C}_{13}\text{H}_{20}\text{OSi}$ $[\text{M}+\text{H}]^+$ 220.38, found: 220.7400; $[\alpha]_{\text{D}}^{20} -15.3$ (c 1.17, CHCl_3).

(14) Has also been reported in a single step from 4-(dimethylphenylsilyl)but-3-yn-2-ol: Lautens, M.; Zhang, C.; Goh, B.; Crudden, C, Johnson, M. *J. Org. Chem.* **1994**, 59, 6208.

(E)-(4S)-2-(dimethylphenylsilane)-2-penten-4-ol (4-methoxy benzyloxy)acetate (8b): **7b** (10 g, 45.4 mmol) was placed in a round bottom flask and dissolved in CH₂Cl₂ (130 mL) and cooled to 0 °C. DCC (14 g, 68.1 mmol) and DMAP (0.66 g, 5.4 mmol) was added followed by slow addition of 4-methoxybenzyloxy acetic acid¹³ (9.35 g, 47.6 mmol) dissolved in CH₂Cl₂ (60 mL) over 15 minutes followed by a CH₂Cl₂ (0.5 mL) rinse. Allow solution to warm to room temperature over night in ice bath. White precipitate is then filtered off and solution concentrated under vacuum. Cloudy yellow/orange oil is then purified using a gradient elution over silica gel (hexanes/ethyl acetate: 98:2; 95:5; 90:10) to give of light yellow to clear oil (16g, 89%). ¹H NMR (CDCl₃, 400 MHz): δ 7.51-7.48 (m, 2H), 7.33-7.30 (m, 3H), 7.26 (d, J = 8.4 Hz, 2H), 6.86 (d, J = 8.4 Hz, 2H), 5.99-5.96 (dq, J = 10 Hz, 1.2 Hz, 1H), 5.45 (dq, J = 10 Hz, 6.4 Hz, 3H), .449 (s, 3H), .409 (s, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 169.2, 159.4, 141.4, 138.2, 138.1, 133.6, 129.6, 129.1, 128.9, 127.7, 113.7, 72.6, 70.8, 66.8, 54.9, 24.8, 20.4, -1.8, -2.1; IR (film) ν_{max} 2949, 1743, 1613, 1512, 1251, 1199, 1120, 831 cm⁻¹; HRMS(CI, NH₃) *m/z* calc'd for C₂₃H₃₀O₄Si [M+H]⁺ 398.5791, found: 398.2578; [α]_D²⁰ +6.92 (c 1.20, CHCl₃).

(E)-(2S,3R) 2-(4-methoxybenzyloxy)-3-(Dimethylphenylsilyl)-3-methyl-4-hexenoic acid (9b): 1M LiHMDS in THF (97.1 mL, 97.1 mmol) was brought to -78 °C. A separate flask containing **8b** (9.68 g, 24.3 mmol) dissolved in THF (120 mL) was slowly added via cannula at -78 °C. The solution was then allowed to stir for an additional 30 minutes at -78 °C. To the orange/yellow solution was added TMSCl (18.5 mL, 146 mmol) over 15 minutes. The clear (sometimes cloudy white) solution is then allowed to warm to ambient temperature on its own and stir at room temperature for approximately 2 hours. At this point a saturated solution of NH₄Cl was added followed by extraction with diethyl ether. The combined organic layers were then dried over MgSO₄, filtered and the solvent evaporated under vacuum to give a light yellow oil. Purification by flash chromatography over silica gel (hexanes/ethyl acetate: 90/10) gives a clear oil (8.5 g, 88%) as a 6:1 to 8:1 diastereomeric mixture of **9b** and **9a**. ¹H NMR (CDCl₃, 400 MHz): δ 7.39 (d, J = 7.6 Hz, 2H), 7.30 (m, 5H), 7.23 (d, J = 6.4 Hz, 2H), 5.82 (d, J = 15.6 Hz, 1H), 5.13 (dq, J = 6.4 Hz, 2.8 Hz, 1H), 4.36 (d, J = 10.4 Hz, 1H), 4.10 (dd, J = 10.4 Hz, 3.6 Hz, 1H), 3.79 (s, 3H), 3.82 (dd, J = 6.4 Hz, 1.2 Hz, 3H), 1.01 (s, 3H), .253 (s, 3H), .191 (s, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 176.1, 159.4, 137.1, 134.8, 131.4, 130.0, 129.2, 128.9, 127.4, 123.1, 113.7, 84.5, 72.2, 55.3, 34.8, 18.5, 16.6, -3.91, -4.10; IR (film) ν_{max} 3069, 2957, 1717, 1612, 1514, 1251, 1113, 814 cm⁻¹ HRMS(CI, NH₃) *m/z* calc'd for C₂₃H₃₀O₄Si [M+H]⁺ 398.1779, found: 398.569.

(E)-(2S, 3R) Methyl 2-(4-methoxybenzyloxy)-3-(Dimethylphenylsilyl) 3'-methyl-4-hexenoate (9e): To a flask with **9b** (10 g, 25.1 mmol) was added a saturated NaHCO₃ solution (80 mL). To a second flask is added Adogen-464[®] (11.2 g, 27.8 mmol) followed by CH₂Cl₂ (85 mL) and iodomethane (2.0 mL, 33 mmol). The second solution containing the adogen/MeI mix is poured into the initial flask in one shot at room temperature followed by a CH₂Cl₂ rinse (2 mL). The heterogeneous mixture is then rapidly stirred at room temperature overnight. The mixture is then diluted with water and extracted with CH₂Cl₂. The extracts are then dried over MgSO₄, filtered and concentration under vacuum to obtain a light yellow oil. The oil may be purified via flash chromatography over silica gel (hexanes/ethyl acetate: 95/5; 90/10) to obtain a clear oil (9.10 g, 88%). ¹H NMR (CDCl₃, 400 MHz): δ 7.37 (d, J = 7.6 Hz, 2H), 7.35-7.25 (m, 5H), 6.87 (d, J = 8.8 Hz, 2H), 5.90 (d, J = 15.6 Hz, 1H), 5.05 (dq, J = 15.6 Hz, 6.4 Hz, 1H), 4.35 (d, J = 10.4 Hz, 1H), 4.03 (d, J = 10.8 Hz, 1H), 3.81 (s, 3H), 3.67 (s, 1H), 3.60 (s, 3H), 1.68 (d, J = 6.4 Hz, 3H), .959 (s, 3H), .233 (s, 3H), .181 (s, 3H); ¹³C NMR (75 MHz, CDCl₃) 171.5, 159.2, 137.2, 134.7, 131.9, 129.9, 129.4, 128.8, 127.2, 122.0, 113.6, 84.7, 71.8, 55.2, 50.9, 34.9, 18.4, 16.5, -4.06, -4.23; IR (film) ν_{max} 2953, 1746, 1730, 1514, 1250, 1111, 813 cm⁻¹; HRMS(Cl, NH₃) *m/z* calc'd for C₂₄H₃₂O₄Si [M+H]⁺ 412.5740, found: 412.5916; [α]_D²⁰ -13.4 (c 1.25, CHCl₃).

(E)-(2S,3R) Methyl 2-hydroxy-3-(Dimethylphenylsilyl)-3-methyl-hex-4-enoate (9f): PMB ester **9e** (8.0 g, 19.4 mmol) was placed in a round bottom flask with CH₂Cl₂ (480 mL) and water (48 mL, 10% by volume) and was cooled to 0 °C. The solution was rapidly stirred while DDQ (9.08 g, 38.8 mmol) was added. Once addition was complete the red/brown solution was stirred at 0 °C for 2 hours then warmed to room temperature and stirred overnight. A saturated solution of NaHCO₃ was added and aqueous layer extracted with CH₂Cl₂ combined with previous organic layer and extracted 2 more times with sat NaHCO₃ solution followed by a brine extraction. Organic layers are then dried over MgSO₄, filtered and concentrated under vacuum to get a orange/brown oil. Purification of the resulting oil over silica gel (hexanes/ethyl acetate: 99:1) resulted in of a clear oil (4.1 g, 72%). Product may solidify on standing, recrystallized with hexanes. ¹H NMR (CDCl₃, 400 MHz): δ 7.50(m, 2H), 7.21(m, 3H), 5.66(d, J = 15.6Hz, 1H), 5.16 (dq, J = 15 Hz, 6.4 Hz, 1H), 3.98 (d, J = 6.8 Hz, 1H), 3.64 (s, 3H), 2.99 (d, J = 6.8 Hz, 1H), 1.68 (dd, 6.4 Hz, 1.6 Hz, 3H), 1.02 (s, 3H), .382 (s, 3H), .303 (s, 3H); ¹³C NMR (75 MHz, CDCl₃) 174.6, 137.3, 134.8, 130.8, 128.8, 127.3, 123.1, 76.6, 51.7, 35.9, 18.4,

16.2, -4.05, -4.47; IR (film) $\nu_{\max}$ 3504, 2955, 1727, 1247 cm^{-1} ; HRMS(Cl, NH_3) m/z calc'd for $\text{C}_{16}\text{H}_{24}\text{O}_3\text{Si}$ $[\text{M}+\text{H}]^+$ 292.450, found: 292.1488; $[\alpha]_{\text{D}}^{20}$ +30.3 (c 1.10, CHCl_3).

(E)-(2S,3R)-Methyl-3-(dimethylphenylsilyl)-3-methyl-2-(trimethylsiloxy)-hex-4-enoate 4b: A solution of α -hydroxysilane **9f** (4.0 g, 13.7 mmol) in CH_2Cl_2 (41 mL) was cooled to -78°C and 2,6-lutidine (3.17 mL, 27.4 mmol) was added. Slow addition of 99% TMSOTf (3.22 mL, 14.4 mmol) then commenced over 15 minutes. The mixture is warmed and stirred at 0°C for 2 hours after which water is added and extracted with CH_2Cl_2 . The combined organic layers are then dried over MgSO_4 , filtered and concentrated under vacuum to get an oil. The oil was then purified over silica gel (hexane/ethyl acetate: 98/2) to get clear oil (4.85 g, 97%). ^1H NMR (CDCl_3 , 400 MHz): δ 7.45 (m, 2H), 7.30 (m, 3H), 5.90 (dd, J = 16.0 Hz, 1.6 Hz, 1H), 4.95 (dq, J = 15.6 Hz, 6.4 Hz, 1H), 4.09 (s, 1H), 3.56 (s, 3H), 1.60 (dd, 6.4 Hz, 2.0 Hz, 3H), .894 (s, 3H), .337 (s, 3H), .270 (s, 3H), .059 (s, 3H), .051 (s, 3H); ^{13}C NMR (75 MHz, CDCl_3): 172.4, 137.6, 134.8, 132.0, 128.8, 127.2, 121.9, 78.3, 50.8, 35.5, 18.3, 16.1, -.133, -3.64, -4.72; IR (film) $\nu_{\max}$ 2956, 1752, 1732, 1252, 1113 cm^{-1} ; HRMS(Cl, NH_3) m/z calc'd for $\text{C}_{19}\text{H}_{32}\text{O}_3\text{Si}_2$ $[\text{M}+\text{H}]^+$ 364.632, found: 364.1866; $[\alpha]_{\text{D}}^{20}$ -.72 (c .42, CHCl_3).

2,2,4,6,6-Pentamethyl-benzo[1,2-d;4,5-d']bis[1,3]dioxole (10a):

2,2,6,6-Tetramethylbenzo [1,2- d ;4,5- d']bis[1,3]dioxole¹⁵ (10 g, 45.0 mmol) was added to a round bottom flask under nitrogen followed by THF (160 mL) and TMEDA (7.47 mL, 49.5 mmol). A 2.5M n -BuLi solution in hexanes (19 mL, 47 mmol) was then slowly added at room temperature with rapid stirring. The cloudy mixture was then brought to reflux for 1 hour before being cooled to room temperature. Iodomethane (2.94 mL, 47.2 mmol) was then added. The solution is then brought to reflux for an additional hour. Cool solution to room temperature and quench with a equal volume of water. Extract aqueous solution with diethyl ether and combine the organics over MgSO_4 . The solution is then filtered and concentrated under vacuum to get a white solid. Column over silica gel (hexanes/ethyl acetate: 90/10) to get a white solid (7.5 g, 71%). ^1H NMR (CDCl_3 , 400 MHz): δ 6.16 (s, 1H), 2.05 (s, 3H), 1.61 (s, 12H); ^{13}C NMR (75 MHz, CDCl_3): δ 139.60, 139.35, 117.20, 103.31, 90.24, 25.57, 8.48; HRMS(Cl, NH_3) m/z calc'd for $\text{C}_{13}\text{H}_{16}\text{O}_4$ $[\text{M}+\text{H}]^+$ 236.2700, found: 236.1070.

(15) Reddy, T. J.; Iwama, T.; Halpern, H. J.; Rawal, V. H. *J. Org. Chem.* **2002**, 67, 4635.

2,2,6,6,8-Pentamethyl-benzo[1,2-d;4,5-d']bis[1,3]dioxole-4-carbaldehyde (10b):

2,2,4,6,6-Pentamethyl-benzo[1,2-d;4,5-d']bis[1,3]dioxole **10a** (6.0 g, 25 mmol) was added to a round bottom flask under nitrogen followed by diethyl ether (90 mL) and TMEDA (5.7 mL, 38 mmol). A 2.5M *n*-BuLi solution in hexanes (15 mL, 38 mmol) was slowly added at room temperature. The solution is then brought to reflux for 1 hour before being re-cooled to ambient temperatures. DMF (7.9 mL, 102 mmol) was then slowly added to the cloudy solution. After addition the colored solution is again brought to reflux for an additional hour. Cool to room temperature and add an equivalent amount of water. The aqueous layer is extracted with ether and combined over MgSO₄. Filter the solution and evaporate under reduced pressure to get an off white solid. Column over silica gel with a gradient elution (hexanes/ethyl acetate: 90/10; 80/20) to obtain a white solid (4.69 g, 69%). ¹H NMR (CDCl₃, 400 MHz): δ 10.02 (s, 1H), 2.09 (s, 3H), 1.66 (s, 12H); ¹³C NMR (75 MHz, CDCl₃): δ 185.15, 139.97, 139.76, 119.60, 110.36, 104.44, 25.65, 9.30; IR (film) $\nu_{\max}$ 2991, 2936, 2855, 2757, 1690 cm⁻¹; HRMS(Cl, NH₃) *m/z* calc'd for C₁₄H₁₆O₅ [M+H]⁺ 264.2806, found: 264.1015.

General procedure for dihydropyran formation

The desired diastereomer of silane **4** was placed in a round bottom flask equipped with a stir bar .05M CH₂Cl₂, and the appropriate aldehyde (1 equiv. aromatic or 1.2 equiv. aliphatic). The mixture is then cooled to -50 °C and TMSOTf (30 mol %) was added all at once. The reaction is allowed to stir for at least¹⁶ 24 hours at -50 °C before a sat solution of NaHCO₃ (equal volume) is added. Once the bicarbonate has been added the solution is allowed to warm to room temperature on its own. The aqueous layer is then extracted with additional CH₂Cl₂ (2x) and placed over MgSO₄. Filter off MgSO₄ and concentrated under vacuum to get a crude oil. See specific aldehyde to determine the appropriate purification techniques.

(2R,5S,6R)-6-Ethyl-3,5-dimethyl-5,6-dihydro-2H-pyran-2-carboxylic acid methyl ester (11a): Further purification over silica gel (hexane/ethyl acetate: 98/2) gives (0.25 g, 91%) of a clear oil (from .050g of **4a** silane). ¹H NMR (CDCl₃, 400 MHz): δ 5.41 (m, 1H), 4.59 (m, 1H), 3.75 (s, 3H), 2.92 (td, J = 8.8 Hz, 2.4 Hz, 1H), 2.20 (m, 1H), 1.78-1.62

(16) Some aldehydes may take longer. Monitoring is advised.

(quint, $J = 7.2$ Hz, 2.4 Hz, 1H), 1.60 (s, 3H), 1.56-1.42 (quint, $J = 7.2$ Hz, 1H), .97 (t, $J = 7.2$ Hz, 3H), .88 (d, $J = 6.8$ Hz, 3H); ^{13}C NMR (75 MHz, CDCl_3): δ 171.1, 129.8, 129.1, 81.5, 79.0, 52.1, 33.5, 25.5, 18.1, 17.4, 10.1; IR (CHCl_3 solution) ν_{max} 3018, 2965, 2876, 1747, 1215, 755 cm^{-1} ; HRMS(CI, NH_3) m/z calc'd for $\text{C}_{11}\text{H}_{18}\text{O}_3$ $[\text{M}+\text{H}]^+$ 198.262, found: 198.1312; $[\alpha]_{\text{D}}^{20} +168.4$ (c .31, CHCl_3).

(2R,5S,6R)-6-Cyclohexyl-3,5-dimethyl-5,6-dihydro-2H-pyran-2-carboxylic acid methyl ester (11b): Further purification over silica gel (hexane/ethyl acetate: 98/2) gives (0.031 g, 89%) a clear oil (from .050g of **4a** silane). ^1H NMR (CDCl_3 , 400 MHz): δ 5.41 (m, 1H), 4.53 (m, 1H), 3.73 (s, 3H), 2.85 (d, $J = 9.6$ Hz, 1H), 2.39 (m, 1H), 1.79-1.60 (br m, 4H), 1.59 (s, 3H), 1.52-1.1 (m, 7H), .86 (d, $J = 7.2$ Hz, 3H); ^{13}C NMR (75 MHz, CDCl_3): δ 171.2, 130.4, 129.1, 83.8, 79.1, 51.2, 38.7, 30.6, 29.9, 26.7, 26.4, 26.3, 25.2, 18.0, 17.4; IR (film) ν_{max} 2929, 2852, 1761, 1742, 1449, 1274, 1166, 1118, 1029 cm^{-1} ; HRMS(CI, NH_3) m/z calc'd for $\text{C}_{15}\text{H}_{24}\text{O}_3$ $[\text{M}+\text{H}]^+$ 252.353, found: 252.171; $[\alpha]_{\text{D}}^{20} +148.5$ (c .68, CHCl_3).

(2R,5S,6R)-3,5-Dimethyl-6-((E)-propenyl)-5,6-dihydro-2H-pyran-2-carboxylic acid methyl ester (11c): Further purification over silica gel (hexane/ethyl acetate: 98/2) gives (0.020 g, 71%) a clear oil (from .050g of **4a** silane). ^1H NMR (CDCl_3 , 400 MHz): δ 5.74 (dq, $J = 15.2$ Hz, 6.0 Hz, 1H), 5.51 (ddq, $J = 15.2$ Hz, 9.2 Hz, 1.6 Hz, 1H), 5.46 (m, 1H), 4.66 (m, 1H), 3.73 (s, 3H), 3.43 (t, $J = 9.2$ Hz, 1H), 2.23 (m, 1H), 1.70 (dd, $J = 6.0$ Hz, 1.6 Hz, 3H), 1.61 (m, 3H), .84 (d, $J = 7.2$ Hz, 3H); ^{13}C NMR (75 MHz, CDCl_3): δ 170.7, 130.8, 129.8, 129.3, 129.0, 81.6, 78.5, 52.2, 33.6, 18.2, 17.8, 17.0; IR (film) ν_{max} 2956, 2873, 1742, 1437, 1274, 1169, 1109, 1029 cm^{-1} ; HRMS(CI, NH_3) m/z calc'd for $\text{C}_{12}\text{H}_{18}\text{O}_3$ $[\text{M}+\text{H}]^+$ 210.273, found: 210.1237; $[\alpha]_{\text{D}}^{20} +147.6$ (c 1.14, CHCl_3).

(2R,5S,6S)-3,5-Dimethyl-6-phenyl-5,6-dihydro-2H-pyran-2-carboxylic acid methyl ester (11d): Further purification over silica gel (hexane/ethyl acetate: 98/2) gives (0.105 g, 85%) a clear oil (from .168g of **4a** silane). ^1H NMR (CDCl_3 , 400 MHz): δ 7.24-7.44 (m, 5H), 5.59 (s, 1H), 4.81 (s, 1H), 4.98 (d, $J = 9.6$ Hz, 1H), 3.75 (s, 1H), 2.52 (m, 1H), 1.70 (s, 3H), .78 (d, $J = 7.2$ Hz, 3H); ^{13}C NMR (75 MHz, CDCl_3): δ 170.9, 140.4, 130.0, 129.5, 128.6, 128.3, 127.7, 83.0, 79.4, 52.4, 35.8, 17.8, 17.1; IR (film) ν_{max} 2955, 2872,

1757, 1740, 1454, 1436, 1198, 1032 cm^{-1} ; HRMS(CI, NH_3) m/z calc'd for $\text{C}_{15}\text{H}_{19}\text{O}_3$ $[\text{M}+\text{H}]^+$ 247.314, found: 274.1354; $[\alpha]_{\text{D}}^{20} +82.2$ (c .63, CHCl_3).

(2R,5S,6S)-3,5-Dimethyl-6-naphthalen-2-yl-5,6-dihydro-2H-pyran-2-carboxylic acid methyl ester (11e): Further purification over silica gel (hexane/ethyl acetate: 98/2) gives (0.115 g, 84%) a clear oil (from .168g of **4a** silane). ^1H NMR (CDCl_3 , 400 MHz): δ 7.85-7.79 (m, 4H), 7.56 (d, J = 8.8 Hz, 1H), 7.45 (m, 2H), 5.63 (s, 1H), 4.85 (s, 1H), 4.16 (d, J = 9.6 Hz), 3.78 (s, 3H), 2.63 (m, 1H), 1.73 (s, 3H), .80 (d, J = 7.2 Hz, 3H); ^{13}C NMR (75 MHz, CDCl_3): δ 170.6, 137.5, 133.3, 133.1, 129.8, 129.2, 128.3, 128.0, 127.7, 126.7, 126.0, 125.9, 125.1, 82.9, 79.1, 52.1, 35.4, 18.2, 16.9; IR (film) ν_{max} 2955, 2873, 1752, 1742, 1436, 1273, 1169, 1109, 819, 732 cm^{-1} ; HRMS(CI, NH_3) m/z calc'd for $\text{C}_{19}\text{H}_{20}\text{O}_3$ $[\text{M}+\text{H}]^+$ 296.366, found: 296.1387; $[\alpha]_{\text{D}}^{20} + 87.7$ (c .561, CHCl_3).

(2R,5S,6S)-6-(2,5-Dimethoxy-phenyl)-3,5-dimethyl-5,6-dihydro-2H-pyran-2-carboxylic acid methyl ester (11f): Further purification over silica gel (hexane/ethyl acetate: 95/5) gives (0.122 g, 80%) a clear oil (from .168g of **4a** silane). ^1H NMR (CDCl_3 , 400 MHz): δ 7.08 (m, 1H), 6.77 (m, 2H), 5.59 (br s, 1H), 4.81 (br s, 1H), 4.59 (d, J = 9.6 Hz, 1H), 3.76 (s, 3H), 3.75 (obsc. s, 3H), 3.74 (obsc. s, 3H), 2.51 (m, 1H), 1.69 (s, 3H), .77 (d, J = 7.6 Hz, 1H); ^{13}C NMR (75 MHz, CDCl_3): δ 170.6, 154.0, 151.2, 130.1, 129.8, 129.1, 113.7, 113.1, 111.8, 79.3, 74.5, 56.0, 55.5, 52.0, 35.7, 18.0, 16.4; IR (film) ν_{max} 2954, 1756, 1742, 1501, 1278, 1216, 1034, 733 cm^{-1} ; HRMS(CI, NH_3) m/z calc'd for $\text{C}_{17}\text{H}_{22}\text{O}_5$ $[\text{M}+\text{H}]^+$ 306.358, found: 306.14786; $[\alpha]_{\text{D}}^{20} +71.2$ (c .25, CHCl_3).

(2R,5S,6S)-6-(4-Chloro-phenyl)-3,5-dimethyl-5,6-dihydro-2H-pyran-2-carboxylic acid methyl ester (11g): Further purification over silica gel (hexane/ethyl acetate: 98/2) gives (0.115 g, 83%) a clear oil (from .168g of **4a** silane). ^1H NMR (CDCl_3 , 400 MHz): δ 7.31 (m, 4H), 5.57 (br. s, 1H), 4.79 (br. s, 1H), 3.95 (d, J = 9.6 Hz, 1H), 3.76 (s, 3H), 2.44 (m, 1H), 1.70 (s, 3H), .77 (d, J = 7.6 Hz, 3H); ^{13}C NMR (75 MHz, CDCl_3): δ 170.8, 139.1, 134.0, 129.8, 129.6, 129.3, 129.1, 128.8, 82.2, 79.3, 52.4, 35.8, 18.5, 17.0; IR

(film) $\nu_{\max}$ 2956, 2874, 1766, 1756, 1492, 1199, 1186, 1090, 812 cm^{-1} ; HRMS(CI, NH_3) m/z calc'd for $\text{C}_{15}\text{H}_{18}\text{O}_3$ $[\text{M}+\text{H}]^+$ 281.7588, found: 281.0912; $[\alpha]_{\text{D}}^{20} +46.9$ (c .56, CHCl_3).

(2R,5S,6S)-3,5-Dimethyl-6-(2,2,6,6,8-pentamethyl-benzo[1,2-d;4,5-d']bis[1,3]dioxol-4-yl)-5,6-dihydro-2H-pyran-2-carboxylic acid methyl ester (11h): Further purification over silica gel (hexane/ethyl acetate: 98/2) gives (0.117 g, 63%) an oil (from .168g of **4a** silane). ^1H NMR (CDCl_3 , 400 MHz): δ 5.56 (m, 1H), 4.81 (br. s, 1H), 4.20 (d, J = 10.4 Hz, 1H), 3.73 (s, 3H), 3.03 (br. s, 1H), 2.02 (s, 3H), 1.66 (s, 3H), 1.62 (s, 6H), 1.60 (s, 6H), .81 (d, J = 7.2 Hz, 3H); ^{13}C NMR (75 MHz, CDCl_3): δ 170.27, 139.42, 138.51, 129.86, 128.95, 117.35, 103.19, 103.00, 79.23, 74.78, 52.07, 31.74, 25.38, 18.13, 16.59, 8.54; IR (film) $\nu_{\max}$ 2991, 1742, 1456, 1093 cm^{-1} ; HRMS(CI, NH_3) m/z calc'd for $\text{C}_{22}\text{H}_{28}\text{O}_7$ $[\text{M}+\text{H}]^+$ 404.4643, found: 404.1820; $[\alpha]_{\text{D}}^{20} +69.6$ (c .76, CHCl_3).

Antipode from **4a'** silane (**11h'**) $[\alpha]_{\text{D}}^{20} -78.4$ (c .70, CHCl_3).

(2S,5S,6S)-6-Ethyl-3,5-dimethyl-5,6-dihydro-2H-pyran-2-carboxylic acid methyl ester (11i): Further purification over silica gel (hexane/ethyl acetate: 98/2) gives (0.066 g, 72%) a clear oil (from .168g of **4b** silane). ^1H NMR (CDCl_3 , 400 MHz): δ 5.72 (d app t, J = 6.4 Hz, 1.2 Hz, 1H), 4.64 (m, 1H), 3.74 (s, 3H), 3.38 (d app t, J = 7.6 Hz, 1.2 Hz, 1H), 1.99 (m, 1H), 1.67-1.56 (d sex, J = 7.6 Hz, 1.2 Hz, 1H), 1.58 (m, 3H), 1.48-1.38 (d sex, J = 7.6 Hz, 2.0 Hz, 1H), .96 (d, J = 7.2 Hz, 3H), .90 (t, J = 7.6 Hz, 3H); ^{13}C NMR (75 MHz, CDCl_3): δ 170.8, 129.9, 128.8, 79.8, 77.7, 52.2, 31.7, 25.0, 18.3, 13.3, 10.3; IR (CHCl_3 solution) $\nu_{\max}$ 2964, 1759, 1741, 1278 cm^{-1} ; HRMS(CI, NH_3) m/z calc'd for $\text{C}_{11}\text{H}_{18}\text{O}_3$ $[\text{M}+\text{H}]^+$ 198.2621, found: 198.0711; $[\alpha]_{\text{D}}^{20} -84.5$ (c 1.53, CHCl_3).

(2S,5S,6S)-6-Cyclohexyl-3,5-dimethyl-5,6-dihydro-2H-pyran-2-carboxylic acid methyl ester (11j): Further purification over silica gel (hexane/ethyl acetate: 98/2) gives (0.092 g, 79%) a clear oil (from .168g of **4b** silane). ^1H NMR (CDCl_3 , 400 MHz): δ 5.72 (d app q, J = 6.4 Hz, 1.6Hz, 1H), 4.60 (br s 1H), 3.74 (s, 3H), 3.06 (dd, J = 9.6 Hz, 2.4

Hz, 1H), 2.10 (m, 2H), 1.70-1.60 (br m, 4H), 1.57 (d, $J = 1.6$ Hz, 3H), 1.54-1.44 (m, 1H), 1.28-1.07 (m, 3H), .97 (d, $J = 6.8$ Hz, 3H), .81 (m, 2H); ^{13}C NMR (75 MHz, CDCl_3): δ 170.9, 130.1, 128.9, 80.8, 80.2, 52.2, 38.2, 30.1, 30.0, 28.3, 26.6, 25.9, 25.6, 18.2, 13.3; IR (film) ν_{max} 2923, 2851, 1759, 1743, 1450, 1277 cm^{-1} ; HRMS(CI, NH_3) m/z calc'd for $\text{C}_{15}\text{H}_{24}\text{O}_3$ $[\text{M}+\text{H}]^+$ 252.3537, found: 252.171; $[\alpha]_{\text{D}}^{20}$ -42.3 (c .30, CHCl_3).

(2S,5S,6R)-3,5-Dimethyl-6-((E)-propenyl)-5,6-dihydro-2H-pyran-2-carboxylic acid methyl ester (11k): Further purification over silica gel (hexane/ethyl acetate: 98/2) gives (0.065 g, 67%) a clear oil (from .168g of **4b** silane). ^1H NMR (CDCl_3 , 400 MHz): δ 5.84-5.79 (dq, $J = 15.2$ Hz, 6.4 Hz, 1H), 5.48 (br d, $J = 1.6$ Hz, 1H), 5.47-5.40 (ddq, $J = 15.2$ Hz, 7.6 Hz, 1.6 Hz, 1H), 4.54 (s, 1H), 3.95 (t, $J = 8.4$ Hz, 1H), 3.73 (s, 3H), 2.08 (m, 1H), 1.74 (s, 3H), 1.71 (dd, $J = 6.8$ Hz, 1.6 Hz, 3H), .860 (d, $J = 7.2$ Hz, 3H); ^{13}C NMR (75 MHz, CDCl_3): δ 171.6, 130.4, 129.9, 129.1, 128.5, 77.9, 75.8, 51.9, 33.8, 19.7, 17.9, 16.9; IR (film) ν_{max} 2957, 2875, 1750, 1676, 1445, 1435, 1111 cm^{-1} ; HRMS(CI, NH_3) m/z calc'd for $\text{C}_{12}\text{H}_{18}\text{O}_3$ $[\text{M}+\text{H}]^+$ 210.2731, found: 210.1338; $[\alpha]_{\text{D}}^{20}$ -129.5 (c .42, CHCl_3).

(2S,5S,6S)-3,5-Dimethyl-6-phenyl-5,6-dihydro-2H-pyran-2-carboxylic acid methyl ester (11l): Further purification over silica gel (hexane/ethyl acetate: 98/2) gives (0.114 g, 92%) a clear oil (from .168g of **4b** silane). ^1H NMR (CDCl_3 , 400 MHz): δ 7.39-7.27 (m, 5H), 5.61 (s, 1H), 4.66 (s, 1H), 4.55 (d, $J = 9.6$ Hz, 1H), 3.75 (s, 3H), 2.44 (m, 1H), 1.81 (s, 3H), .80 (d, $J = 6.8$ Hz, 3H); ^{13}C NMR (75 MHz, CDCl_3): δ 171.7, 140.3, 129.7, 128.8, 128.4, 128.1, 127.6, 79.6, 76.5, 51.8, 35.1, 19.5, 16.6; IR (film) ν_{max} 2955, 1747, 1454, 1110 cm^{-1} ; HRMS(CI, NH_3) m/z calc'd for $\text{C}_{15}\text{H}_{19}\text{O}_3$ $[\text{M}+\text{H}]^+$ 247.3141, found: 274.1362; $[\alpha]_{\text{D}}^{20}$ -100.9 (c 1.41, CHCl_3).

(2S,5S,6S)-3,5-Dimethyl-6-naphthalen-2-yl-5,6-dihydro-2H-pyran-2-carboxylic acid methyl ester (11m): Further purification over silica gel (hexane/ethyl acetate: 98/2) gives (0.119 g, 87%) of a clear oil (from .168g of **4b** silane). ^1H NMR (CDCl_3 , 400 MHz): δ 7.81 (m, 4H), 7.52 (d, $J = 8.8$ Hz, 1H), 7.45 (m, 2H), 5.64 (d, $J = 1.6$ Hz, 1H), 4.73 (d, $J = 9.2$ Hz, 1H), 4.71 (s, 1H), 3.77 (s, 3H), 2.55 (m, 1H), 1.84 (s, 3H), .835 (d, $J = 7.2$ Hz, 3H); ^{13}C NMR (75 MHz, CDCl_3): δ 171.6, 137.7, 133.3, 133.1, 129.6, 128.8, 128.2, 128.0, 127.6, 126.9, 125.9, 125.8, 125.2, 79.8, 76.5, 51.9, 35.2, 19.7, 16.8; IR (film) ν_{max}

2955, 1742, 1107, 909, 732 cm^{-1} ; HRMS(CI, NH_3) m/z calc'd for $\text{C}_{19}\text{H}_{20}\text{O}_3$ $[\text{M}+\text{H}]^+$ 296.366, found: 296.1399; $[\alpha]_{\text{D}}^{20}$ -80.0 (c 1.36, CHCl_3).

(2S,5S,6S)-6-(2,5-Dimethoxy-phenyl)-3,5-dimethyl-5,6-dihydro-2H-pyran-2-carboxylic acid methyl ester (11n): Further purification over silica gel (hexane/ethyl acetate: 95/5) gives (0.122 g, 80%) a clear oil (from .168g of **4b** silane). ^1H NMR (CDCl_3 , 400 MHz): δ 6.95 (d, J = 3.2 Hz, 1H), 6.82-6.76 (m, 2H), 5.61 (br s, 1H), 5.06 (d, J = 9.2 Hz, 1H), 4.65 (s, 1H), 3.76 (s, 3H), 3.74 (s, 3H), 3.73 (s, 3H), 2.40 (m, 1H), 1.80 (s, 3H), .78 (d, J = 7.2 Hz, 3H); ^{13}C NMR (75 MHz, CDCl_3): δ 171.7, 154.1, 151.7, 130.3, 130.1, 128.7, 114.0, 113.0, 112.7, 76.6, 72.3, 56.6, 55.6, 51.8, 35.8, 19.5, 16.3; IR (film) ν_{max} 2954, 1748, 1502, 1216, 732 cm^{-1} ; HRMS(CI, NH_3) m/z calc'd for $\text{C}_{17}\text{H}_{22}\text{O}_5$ $[\text{M}+\text{H}]^+$ 306.3586, found: 306.1445; $[\alpha]_{\text{D}}^{20}$ -74.9 (c .975, CHCl_3).

(2S,5S,6S)-6-(4-Chloro-phenyl)-3,5-dimethyl-5,6-dihydro-2H-pyran-2-carboxylic acid methyl ester (11o): Further purification over silica gel (hexane/ethyl acetate: 98/2) gives (0.120 g, 87%) a clear oil (from .168g of **4b** silane). ^1H NMR (CDCl_3 , 400 MHz): δ 7.31 (m, 4H), 5.59 (s, 1H), 4.64 (s, 1H), 4.53 (d, J = 9.6 Hz, 1H), 3.74 (s, 3H), 2.36 (m, 1H), 1.80 (s, 3H), .79 (d, J = 7.6 Hz, 3H); ^{13}C NMR (75 MHz, CDCl_3): δ 171.7, 138.9, 133.8, 129.5, 129.0, 128.8, 128.6, 78.9, 76.4, 51.9, 35.2, 19.5, 16.5; IR (film) ν_{max} 2956, 1740, 1492, 1253, 1110 cm^{-1} ; HRMS(CI, NH_3) m/z calc'd for $\text{C}_{15}\text{H}_{18}\text{ClO}_3$ $[\text{M}+\text{H}]^+$ 281.7588, found: 281.0978; $[\alpha]_{\text{D}}^{20}$ -98.6 (c 1.45, CHCl_3).

(2S,5S,6S)-3,5-Dimethyl-6-(2,2,6,6,8-pentamethyl-benzo[1,2-d;4,5-d']bis[1,3]dioxol-4-yl)-5,6-dihydro-2H-pyran-2-carboxylic acid methyl ester (11p): 1 equiv. of trifluoromethanesulfonic acid was used (instead of TMSOTf) at -78 $^{\circ}\text{C}$ for 24 hours for this substrate. Further purification over silica gel (hexane/ethyl acetate: 98/2) gives (0.084 g, 45%) an oil (from .168g of **4b** silane). ^1H NMR (CDCl_3 , 400 MHz): δ 5.57 (d, J

= 1.6 Hz, 1H), 4.65 (obs. d, $J = 10.2$ Hz, 1H), 4.64 (s, 1H), 3.74 (s, 3H), 2.83 (m, 1H), 2.03 (s, 3H), 1.78 (s, 3H), 1.61 (s, 6H), 1.60 (s, 6H), .81 (d, $J = 7.2$ Hz, 1H); ^{13}C NMR (75 MHz, CDCl_3): δ 171.48, 139.41, 138.67, 129.91, 128.86, 117.28, 103.45, 103.28, 76.70, 72.26, 51.81, 32.23, 25.65, 25.58, 19.70, 16.48, 8.77; IR (film) ν_{max} 2989, 1750, 1737, 1456, 1092 cm^{-1} ; HRMS(Cl, NH_3) m/z calc'd for $\text{C}_{22}\text{H}_{28}\text{O}_7$ $[\text{M}+\text{H}]^+$ 404.4643, found: 404.1827; $[\alpha]_{\text{D}}^{20}$ -51.7 (c .96, CHCl_3).

Assignment of Relative Stereochemistry

The relative stereochemistry of several dihydropyrans were determined by ^1H NMR analysis by n.O.e. The *cis*-dihydropyrans derived from **4a** have a strong n.O.e between H_a and H_b for each example (generally 10%). There was also a weaker n.O.e observed between H_a and the C5 methyl (generally 5%). In all cases the H_a proton also showed a strong n.O.e with the adjacent R group (generally 10%). The *trans*-dihydropyrans derived from **4b** have a n.O.e between H_a and the C5 methyl (generally 4%). There was also an observable n.O.e between H_a and R (generally >5%). The diastereomers resulting from the annulation utilizing aliphatic aldehydes and **4b** showed a strong n.O.e between H_a and H_b (generally 10%). There was also an n.O.e observed between H_a and H_c (generally 5%) and H_a with R (generally 5%).

Observed n.O.e signal of dihydropyrans derived from 4a

R = C_6H_{11} **11b**
 R = C_3H_5 **11c**
 R = C_6H_5 **11d**
 R = $\text{C}_{11}\text{H}_{15}\text{O}_4$ **13**

Observed n.O.e signal of dihydropyrans derived from 4b

R = C_3H_5 **11k**
 R = C_6H_5 **11l**

R = C_2H_5 **11i**
 R = C_6H_{11} **11j**

Synthesis of the C1a-C10 fragment of kendomycin

1,2,4,5-Tetramethoxy-3-methyl-benzene (12a): 1,2,4,5-Tetramethoxybenzene¹⁷ (10 g, 50.4 mmol) was added to a round bottom flask under nitrogen followed by THF (200 mL) and TMEDA (8.38 mL, 55.5 mmol). A 2.5M *n*-BuLi solution in hexanes (21 mL, 53 mmol) was then slowly added at room temperature with rapid stirring. The cloudy mixture was then brought to reflux for 1 hour before being cooled to room temperature. Iodomethane (3.30 mL, 53 mmol) was then added. The solution is then brought to reflux for an additional hour. Cool solution to room temperature and quench with an equal volume of water. Extract aqueous solution with diethyl ether and combine the organics over MgSO₄. The solution is then filtered and concentrated to get a white solid. Column over silica gel with 90/10 hexanes/ethyl acetate to get a white solid (7.59 g, 71%). ¹H NMR (CDCl₃, 400 MHz): δ 6.33 (s, 1H), 3.83 (s, 6H), 3.72 (s, 6H), 2.19 (s, 3H); ¹³C NMR (75 MHz, CDCl₃): δ 148.8, 141.1, 126.1, 96.4, 60.3, 56.1, 9.22; HRMS(CI, NH₃) *m/z* calc'd for C₁₁H₁₆O₄ [M+H]⁺ 212.2456, found: 212.1034.

2,3,5,6-Tetramethoxy-4-methyl-benzaldehyde (12b): 1,2,4,5-Tetramethoxy-3-methylbenzene **12a** (10 g, 47.1 mmol) was added to a round bottom flask under nitrogen followed by diethyl ether (160 mL) and TMEDA (14.2 mL, 94.2 mmol). A 2.5M *n*-BuLi solution in hexanes (38 mL, 94 mmol) was slowly added at room temperature. The solution is then brought to reflux for 1 hour before being re-cooled to ambient temperatures. DMF (14.6 mL, 188 mmol) was then slowly added to the cloudy solution. After addition the colored solution is again brought to reflux for an additional hour. Cool to room temperature and add an equivalent amount of water. The aqueous layer is the extracted with ether and combined over MgSO₄. Filter the solution and evaporate under reduced pressure to get an off white solid. Column over silica gel with a gradient (hexanes/ethyl acetate: 90/10; 80/20) to obtain a white solid (8.02 g, 71%). ¹H NMR (CDCl₃, 400 MHz): δ 10.3 (s, 1H), 3.87 (s, 6H), 3.79 (s, 6H), 2.21 (s, 3H); ¹³C NMR (75 MHz, CDCl₃): δ 189.1, 150.6, 147.9, 134.1, 121.6; IR (film) *v*_{max} 2941, 2844, 1692, 1465, 1081, 1018 cm⁻¹; HRMS(CI, NH₃) *m/z* calc'd for C₁₂H₁₆O₅ [M+H]⁺ 240.2560, found: 240.0972.

(17) Poigny, S.; Guyot, M.; Samadi, M. *Tetrahedron* **1998**, *54*, 14791.

(2S,5R,6R)-3,5-Dimethyl-6-(2,3,5,6-tetramethoxy-4-methyl-phenyl)-5,6-dihydro-2H-pyran-2-carboxylic acid methyl ester 13: Silane **4a'** (5 g, 13.7 mmol) and aldehyde **12b** (3.13 g, 13.7 mmol) were placed in a round bottom flask under a nitrogen atmosphere equipped with a magnetic stir bar. Anhydrous methylene chloride (200 mL) was then added and the solution was cooled to -50 °C. At this point TMSOTf (0.720 mL, 30 mol %) was added in one portion and the solution was allowed to stir at this temperature overnight. Saturated NaHCO₃ solution was added and the mixture allowed to warm to room temperature over 1hr. Extract aqueous layer with methylene chloride and dry over MgSO₄, filter and concentrated to get a yellow/orange oil. Purification over silica gel (hexane/ethyl acetate: 95/5) afforded of a clear oil (4.52 g, 86.8%). ¹H NMR (CDCl₃, 400 MHz): δ 5.6 (s, 1H), 4.79 (s, 1H), 4.56-4.53 (d, J = 10 Hz, 1H), 3.89 (s, 3H), 3.78 (s, 3H), 3.76 (s, 3H), 3.75 (s, 3H), 3.72 (s, 3H), 3.30 (br m, 1H), 2.14 (s, 3H), 1.68 (s, 3H). ¹³C NMR (75 MHz, CDCl₃): δ, 170.5, 130.6, 128.4, 126.1, 124.1, 79.2, 75.4, 61.4, 60.9, 60.0, 51.8, 31.4, 18.2, 17.4, 9.15; IR (film) ν_{max} 2938, 1743, 1465, 1408, 1369, 1267, 1088, 733 cm⁻¹; HRMS(Cl, NH₃) *m/z* calc'd for C₂₀H₂₈O₇ [M+H]⁺ 380.4381, found: 380.1906; [α]_D²⁰ -59.1 (c 1.23, CHCl₃).

(1S,2S,4R,5S)-1,5-Dimethyl-4-(2,3,5,6-tetramethoxy-4-methyl-phenyl)-3,7-dioxabicyclo[4.1.0]heptane-2-carboxylic acid methyl ester (14): **13** (1.5 g, 3.9mmol) and acetonitrile (100 mL) was added to a round bottom flask and cooled to -20 °C. A .0004M aqueous EDTA solution (30 mL) was then added followed by 1,1,1-trifluoroacetone (22 mL, 197mmol). A mixture of Oxone® (12.1 g, 20 mmol) and NaHCO₃ (2.6 g, 31.5 mmol) was added portion-wise over 15 minutes. The reaction was allowed to stir for 2 hours at -20 °C before being poured into water. The mixture was then extracted with CH₂Cl₂ and dried over MgSO₄. On removal of the solvent a yellow oil remained which, solidified upon standing. Purification via column chromatography using a gradient elution (hexane/ethyl acetate: 95/5; 90/10; 80/20) yielded a white solid (1.33 g, 81%). (0.150 g, 10% of the minor diastereomer was obtained.)

Major isomer (**14**): ^1H NMR (CDCl_3 , 400 MHz): δ 4.43 (s, 1H), 4.33-4.31 (d, 1H J = 10.8 Hz, 1H), 3.89 (br s, 3H), 3.77 (br s, 6H), 3.75 (s, 3H), 3.02-2.97 (m, J = 7.6 Hz, 1H), 2.89 (s, 1H), 2.13 (s, 3H), 1.48 (s, 3H), .894-.875 (d, J = 7.6 Hz, 3H); ^{13}C NMR (75 MHz, CDCl_3): δ , 169.78, 149.03, 148.56, 147.93, 147.29, 126.41, 123.38, 79.17, 70.42, 64.14, 61.50, 60.99, 60.12, 58.78, 51.91, 31.70, 19.88, 14.05, 9.30; HRMS(CI, NH_3) m/z calc'd for $\text{C}_{20}\text{H}_{28}\text{O}_8$ $[\text{M}+\text{H}]^+$ 396.4375, found: 396.1871; $[\alpha]_{\text{D}}^{20}$ +6.25 (c 1.6, CHCl_3).

Minor isomer (**14b**): ^1H NMR (CDCl_3 , 400 MHz): δ 4.59 (d, J = 10 Hz, 1H), 4.54 (s, 1H), 3.89 (br s, 3H), 3.78 (br s, 3H), 3.74 (s, 6H), 3.73 (br s, 3H), 3.15-3.11 (ob m, 1H), 3.12 (s, 1H), 2.13 (s, 3H), 1.34 (s, 3H), .87 (d, J = 7.2 Hz, 3H); ^{13}C NMR (75 MHz, CDCl_3): δ , 168.9, 148.9, 148.7, 147.4, 147.1, 126.5, 123.6, 77.9, 75.4, 64.4, 61.4, 61.0, 60.1, 54.1, 52.2, 30.6, 18.9, 15.8, 9.3; IR (film) ν_{max} : 2937, 1759, 1565, 1267 1083 cm^{-1} ; HRMS(CI, NH_3) m/z calc'd for $\text{C}_{20}\text{H}_{28}\text{O}_8$ $[\text{M}+\text{H}]^+$ 396.4375, found: ; $[\alpha]_{\text{D}}^{20}$ -3.83 (c 1.2, CHCl_3).

(4R,5R,6R)-4-Hydroxy-3,5-dimethyl-6-(2,3,5,6-tetramethoxy-4-methyl-phenyl)-5,6-dihydro-4H-pyran-2-carboxylic acid methyl ester (15): Epoxide **14** (1.70 g, 4.29 mmol) was added to a round bottom flask along with methanol (43 mL) at which time potassium carbonate (2.96 g, 21.4 mmol) was added. The reaction was allowed to stir overnight at room temperature. The solution was diluted with CH_2Cl_2 and 5% HCl solution and stirred for 1 hour. The entire solution was extracted 3 times with CH_2Cl_2 . The extracts were then washed with water and brine, dried over MgSO_4 , filtered and concentrated to give an oil. Purification may be achieved with a short plug (hexane/ethyl acetate: 80/20) to give a clear oil (1.16 g, 69%). ^1H NMR (CDCl_3 , 400 MHz): δ 5.04-5.01 (d, J = 11.2 Hz, 1H), 3.87-3.84 (br tr, J = 7.2 Hz, 1H), 3.79 (s, 6H), 3.75 (s, 6H), 3.69 (s, 3H), 2.69-2.59 (m, 1H), 2.14 (s, 3H), 2.06 (s, 3H), 1.75-1.73 (br d, J = 5.6 Hz, 1H), .842-.825 (d, J = 6.8 Hz, 3H); ^{13}C NMR (75 MHz, CDCl_3): δ 164.2, 148.4, 147.9, 140.8, 126.8, 122.5, 121.4, 75.5, 74.9, 61.0, 60.2, 51.7, 38.4, 14.9, 13.9, 9.3; IR (film) ν_{max} 3443, 2939, 1725, 1638, 1466, 733 cm^{-1} ; HRMS(CI, NH_3) m/z calc'd for $\text{C}_{20}\text{H}_{28}\text{O}_8$ $[\text{M}+\text{H}]^+$ 396.4375, found: 396.1871; $[\alpha]_{\text{D}}^{20}$ +12.9 (c 14.7, CHCl_3).

(4S,5R,6R)-4-Hydroxy-3,5-dimethyl-6-(2,3,5,6-tetramethoxy-4-methyl-phenyl)-5,6-dihydro-4H-pyran-2-carboxylic acid methyl ester (15a): The minor epoxide **14a** (1.70 g, 4.29 mmol) was added to a round bottom flask along with methanol (43 mL) at which time potassium carbonate (2.96 g, 21.4 mmol) was added. The reaction was allowed to stir overnight at room temperature. The solution was diluted with CH₂Cl₂ and 5% HCl solution and stirred for 1 hour. The entire solution was extracted 3 times with CH₂Cl₂. The extracts were then washed with water and brine, dried over MgSO₄, filtered and concentrated to give an oil. Purification may be achieved with a short silica plug (hexane/ethyl acetate: 80/20) to give a clear oil (1.16 g, 69%). ¹H NMR (CDCl₃, 400 MHz): δ 5.12 (d, J = 11.2 Hz, 1H), 3.89 (d, J = 3.2 Hz, 1H), 3.80 (s, 6H), 3.77 (s, 6H), 3.71 (s, 3H), 2.72 (m, 1H), 2.16 (s, 3H), 2.14 (s, 3H), 1.68 (br s, 1H), .79 (d, J = 6.8 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃): δ 164.30, 148.62, 147.88, 141.14, 126.66, 122.77, 118.97, 77.14, 70.73, 61.05, 60.21, 51.79, 35.15, 16.82, 12.01, 9.35; IR (film) ν_{max} 3488, 2938, 1726, 1640, 1466, 1072 cm⁻¹; HRMS(Cl, NH₃) *m/z* calc'd for C₂₀H₂₈O₈ [M+H]⁺ 396.4375, found: 396.9676; [α]_D²⁰ -69.5 (c 2.1, CHCl₃).

(5S,6R)-3,5-Dimethyl-4-oxo-6-(2,3,5,6-tetramethoxy-4-methyl-phenyl)-5,6-dihydro-4H-pyran-2-carboxylic acid methyl ester (15b): CH₂Cl₂ (6.0 mL) was added into a round bottom flask and cooled to -78 °C. DMSO (1.00 mL, 14.7 mmol) was then added followed by the slow addition of oxalyl chloride (0.64 mL, 7.26 mmol). The solution was allowed to stir for 15 minutes before a solution of the minor isomer of the secondary alcohol **15a** (0.90 g, 2.27 mmol) in CH₂Cl₂ (5 mL) was introduced. The solution was stirred at this temperature for 1 hour at which time triethyl amine (4.00 mL, 29.5 mmol) was added. The solution was stirred here for 15 minutes and allowed to warm to room temperature on its own. A brine solution was then added and was further extracted using CH₂Cl₂. The extracts were combined and dried over MgSO₄, filtered and concentrated to give a solid. Column over silica gel to get a white solid (0.816g 91%). ¹H NMR (CDCl₃, 400 MHz): δ 5.49-5.45 (d, J = 14.4 Hz, 1H), 3.82 (s, 6H), 3.79 (s, 3H), 3.77 (s, 6H), 3.55-3.49 (m, J = 7.2 Hz, 1H), 2.17 (s, 3H), 2.00 (s, 3H), .912-.896 (d, J = 6.4 Hz 3H); ¹³C NMR (75 MHz, CDCl₃): δ 197.2, 163.6, 155.5, 148.4, 147.9, 127.9, 120.9, 115.8, 78.8, 60.9, 60.1, 52.4, 41.7, 10.2, 9.77, 9.22; IR (film) ν_{max} 2938, 1737, 1678, 1612, 1467, 1408, 1233, 1080, 772 cm⁻¹; HRMS(Cl, NH₃) *m/z* calc'd for C₂₀H₂₆O₈ [M+H]⁺ 394.4216, found: 394.1725; [α]_D²⁰ -24.5 (c .66, CHCl₃).

(4R,5R,6R)-4-Hydroxy-3,5-dimethyl-6-(2,3,5,6-tetramethoxy-4-methyl-phenyl)-5,6-dihydro-4H-pyran-2-carboxylic acid methyl ester (15): Esterketopyran **15b** (0.520 g, 1.32 mmol) was placed in a round bottom flask with methanol (13 mL) and $\text{CeCl}_3 \cdot 7\text{H}_2\text{O}$ (0.491 g, 1.32 mmol). The mixture was cooled to -78°C and NaBH_4 (0.052 g, 1.32 mmol) was added in one shot. The reaction was allowed to stir at -78°C for 3 hours before 2 more equivalents of NaBH_4 was added and the solution allowed to warm too room temperature. Water was added and the solution extracted with CH_2Cl_2 and rinsed several times with water and brine. Organics were combined over MgSO_4 filtered and concentrated. Purification may be achieved with a short plug over silica (hexane/ethyl acetate: 80/20) to give a clear oil (0.468 g, 90%). (See above for **15**)

(2S,3R,4R,5R,6R)-4-Hydroxy-3,5-dimethyl-6-(2,3,5,6-tetramethoxy-4-methyl-phenyl)-tetrahydro-pyran-2-carboxylic acid methyl ester (16): Pyran **15** (1.8 g, 4.5 mmol) was added to a round bottom flask followed by methanol (4.5 mL). 10% Pd on carbon (0.45 g) was added and the reaction purged with hydrogen. Allow to stir at room temperature for 4 hours and filter through a plug of celite. The solution was concentrated to get a clear oil (1.79 g, 99%). Crude NMR showed no need for further purification. ^1H NMR (CDCl_3 , 400 MHz): δ 4.48-4.46 (d, $J = 7.2$ Hz, 1H), 4.24 (d, $J = 2.0$ Hz 1H), 3.93 (s, 3H), 3.78 (obsc. s, 3H), 3.77 (obsc. s, 3H), 3.72 (obsc. s, 3H), 3.71 (obsc. s, 3H), 3.60-3.57 (dd, $J = 10.4$ Hz, 4.8 Hz, 1H), 2.59-2.49 (m, 1H), 2.14 (s, 3H), 1.05 (d, $J = 7.2$ Hz, 3H), .75 (d, $J = 6.8$ Hz, 3H); ^{13}C NMR (75 MHz, CDCl_3): δ 170.73, 148.46, 148.30, 147.13, 146.80, 125.84, 123.74, 78.34, 76.37(obs.), 76.33, 70.00, 60.58, 59.89, 59.75, 51.58, 37.61, 34.46, 13.44, 8.96, 6.64.; IR (film) ν_{max} 3490, 2939, 1756, 1464, 1077 cm^{-1} ; HRMS(CI, NH_3) m/z calc'd for $\text{C}_{20}\text{H}_{30}\text{O}_8$ $[\text{M}+\text{H}]^+$ 398.453, found: 398; $[\alpha]_{\text{D}}^{20} +49.8$ (c 1.5, CHCl_3).

Determination of absolute stereochemistry of (16).

The absolute stereochemistry was assigned by Mosher analysis after the conversion of **16** to both (*R*)- and (*S*)-mandelate esters.¹⁸ Comparison of ¹H NMR spectra of each derived mandelate ester established the configuration at the carbinol center to be (*R*). This allowed for the extrapolation of the single point result with the relative stereochemistry as determined by n.O.e to give an absolute configuration of **16** to be (2*S*,3*R*,4*R*,5*R*,6*R*).

Preparation of (*R*)-APA ester (16a).

(2*S*,3*R*,4*R*,5*R*,6*R*)-4-[2-((*R*)-Acetoxy)-2-phenyl-acetoxy]-3,5-dimethyl-6-(2,3,5,6-tetramethoxy-4-methyl-phenyl)-tetrahydro-pyran-2-carboxylic acid methyl ester (16a): **16** (31 mg, .078 mmol) was dissolved in CH₂Cl₂ (1.0 mL) followed by the addition of DCC (22.0 mg, .105 mmol) and a catalytic amount of DMAP (1mg). The solution was cooled to 0 °C and a solution of (*R*)-acetoxymandelic acid (15 mg, .078 mmol) in CH₂Cl₂ (0.5 mL) was slowly added. The reaction was allowed to warm to room temperature on its own overnight before being filtered through celite and concentrated in vacuo. The residue was purified over silica gel (hexanes/ethyl acetate: 98/2) to get a clear oil. ¹H NMR (CDCl₃, 400 MHz): δ 7.47 (m, 2H), 7.37 (m, 3H), 5.89 (s, 1H), 4.88 (dd, *J* = 10.8 Hz, 4.8 Hz, 1H), 4.53 (d, *J* = 10.8 Hz, 1H), 4.23 (d, *J* = 2.8 Hz, 1H), 3.91 (s, 3H), 3.78 (s, 3H), 3.75 (s, 3H), 3.71 (s, 3H), 3.66 (s, 3H), 2.78 (m, 1H), 2.35 (m, 1H), 2.19 (s, 3H), 2.14 (s, 3H), .71 (d, *J* = 6.8 Hz, 3H), .66 (d, *J* = 6.8 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃): δ 170.37, 170.22, 168.32, 148.71, 148.67, 147.49, 147.23, 133.75, 129.31, 128.82, 127.59, 126.46, 123.46, 79.39, 78.08, 77.27, 74.68, 61.39, 60.81, 60.26, 60.02, 51.86, 35.09, 32.26, 20.70, 13.43, 9.28, 7.21; IR (film) ν_{max} 2940,1750,1232,1078 cm⁻¹; HRMS(CI, NH₃) *m/z* calc'd for C₃₀H₃₈O₁₁ [M+H]⁺ 574.6308, found: 574.2414; [α]_D²⁰ +16.06 (*c* 1.60, CHCl₃).

(18) For recent examples of determination of absolute stereochemistry using (*S*)- and (*R*)-AMA a) Cooksey, J.; Gunn, A.; Kocienski, P. J.; Kuhl, A.; Uppal, S.; Christopher, J. A.; Bell, R. *Org. & Biomol. Chem.* **2004**, 2, 1719. b) Alcaide, B.; Almendros, P.; Alonso, J. M.; Aly, M. F. *Chemistry--A European Journal.* **2003**, 9, 3415.

Preparation of (S)-APA ester (16b).

(2S,3R,4R,5R,6R)-4-[2-((S)-Acetoxy)-2-phenyl-acetoxy]-3,5-dimethyl-6-(2,3,5,6-tetramethoxy-4-methyl-phenyl)-tetrahydro-pyran-2-carboxylic acid methyl ester (16b): **16** (37 mg, .093 mmol) was dissolved in CH₂Cl₂ (1.2 mL) followed by the addition of DCC (26 mg, 0.125 mmol) and a catalytic amount of DMAP (1 mg). The solution was cooled to 0 °C and a solution of (S)-acetoxymandelic acid (18 mg, .093 mmol) in CH₂Cl₂ (0.6 mL) was slowly added. The reaction was allowed to warm to room temperature on its own overnight before being filtered through celite and concentrated in vacuo. The residue was purified over silica gel (hexanes:ethyl acetate: 98:2) to get a clear oil. ¹H NMR (CDCl₃, 400 MHz): δ 7.46 (m, 2H), 7.33 (m, 3H), 5.88 (s, 1H), 4.76 (dd, J = 10.8 Hz, 4.8 Hz, 1H), 4.48 (d, J = 10.4 Hz, 1H), 4.26 (d, J = 2.4 Hz, 1H), 3.94 (s, 3H), 3.77 (s, 3H), 3.71 (s, 3H), 3.70 (s, 3H), 3.69 (s, 3H), 2.72 (m, 1H), 2.65 (s, 1H), 2.19 (s, 3H), 2.12 (s, 3H), 1.06 (d, J = 6.8 Hz, 3H), .29 (d, J = 6.8 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃): δ 170.41, 170.20, 168.43, 148.70, 148.65, 147.44, 147.18, 133.70, 129.26, 128.73, 127.57, 126.39, 123.46, 79.94, 78.05, 77.12, 74.77, 61.46, 60.79, 60.25, 60.01, 51.86, 35.15, 32.16, 20.69, 13.07, 9.26, 7.59; IR (film) ν_{max} 2940, 1747, 1232, 1077 cm⁻¹; HRMS(CI, NH₃) *m/z* calc'd for C₃₀H₃₈O₁₁ [M+H]⁺ 574.6308, found: 574.2427; [α]_D²⁰ +50.58 (c 1.20, CHCl₃).

(2S,3S,4R,5S,6R)-4-(tert-Butyl-dimethyl-silanyloxy)-3,5-dimethyl-6-(2,3,5,6-tetramethoxy-4-methyl-phenyl)-tetrahydro-pyran-2-carboxylic acid methyl ester (16c): **16** (1.16 g, 2.92 mmol) was added to a round bottom flask followed by CH_2Cl_2 (12 mL). The flask is then cooled to -78°C and 2,6-lutidine (0.510 mL, 4.38 mmol) was added followed by slow addition of TMSOTf (0.802 mL, 2.5 mmol). After addition was complete stir for 1 hour at -78°C before warm to 0°C and stirred for an additional hour. A saturated NaHCO_3 solution was then added and the aqueous layer extracted with CH_2Cl_2 and combined over MgSO_4 , filtered and concentrated to get an oil. Column over silica gel (hexanes/ethyl acetate: 95/5; 90/10) to get a clear oil (1.31 g, 88%). ^1H NMR (CDCl_3 , 400 MHz): δ 4.47-4.45 (d, $J = 10.8$ Hz, 1H), 4.23 (d, $J = 2.4$ Hz, 1H), 3.94 (s, 3H), 3.78 (s, 3H), 3.77 (s, 3H), 3.72 (s, 3H), 3.71 (s, 3H), 3.55-3.51 (dd, $J = 10.2$ Hz, 4.8 Hz, 1H), 2.59-2.49 (m, 1H), 2.25-2.22 (m, 1H), 2.13 (s, 3H), 1.04 (d, $J = 7.2$ Hz, 3H), .896 (s, 9H), .65 (d, $J = 6.8$ Hz, 3H), .092 (s, 3H), .072 (s, 3H); ^{13}C NMR (75 MHz, CDCl_3): δ 171.1, 148.8, 148.6, 147.4, 147.1, 125.9, 124.4, 78.7, 77.5, 61.3, 60.9, 60.2, 60.0, 51.8, 38.7, 34.9, 25.8, 18.2, 14.3, 9.2, 7.1, -4.2, -4.8; IR (film) ν_{max} 2935, 1762, 1464, 1265, 1077cm^{-1} ; HRMS(CI, NH_3) m/z calc'd for $\text{C}_{26}\text{H}_{44}\text{O}_8\text{Si}$ $[\text{M}+\text{H}]^+$ 512.7161, found: 512.2746; $[\alpha]_{\text{D}}^{20} +62.9$ (c 2.3, CHCl_3).

(2S,3S,4R,5S,6R)-4-(tert-Butyl-dimethyl-silanyloxy)-3,5-dimethyl-6-(2,3,5,6-tetramethoxy-4-methyl-phenyl)-tetrahydro-pyran-2-carbaldehyde (17): Ester **16c** (0.410 g, .80 mmol) was added to a round bottom flask under nitrogen followed by diethyl ether (8.0 mL). The solution was cooled to -78°C before 1M DIBAL-H (3.2 mL, 3.2 mmol) was added over 10 minutes. The reaction was stirred for approximately 2 hours before adding methanol followed by a saturated solution of Rochelle's salt. The solution was allowed to warm to room temperature and was stirred here until turbidity decreased. After extracting with diethyl ether the combined organics were again extracted with Rochelle's salt water then brine. Dry over MgSO_4 , filter and evaporate under reduced pressure to get an oil. Column over silica gel (hexanes/ethyl acetate: 95/5; 90/10; 80/20) to get (0.375g, 91%) of a clear oil. ^1H NMR (CDCl_3 , 400 MHz): δ 4.54-4.52 (d, $J = 10.4$ Hz, 1H), 3.99 (d, $J = 2.0$ Hz, 1H), 3.89 (s, 3H), 3.788 (obsc. s, 3H), 3.787 (obsc. s,

3H), 3.75 (s, 3H), 3.52-3.45 (dd, $J = 10$ Hz, 4.8 Hz, 1H), 2.62-2.55 (m, 1H), 2.3-2.26 (m, 1H), 2.16 (s, 3H), 1.06 (d, $J = 6.8$ Hz, 3H), .892 (s, 9H), .67 (d, $J = 6.8$ Hz, 3H) .081 (s, 3H), .067 (s, 3H); ^{13}C NMR (75 MHz, CDCl_3): δ 202.9, 148.7, 148.6, 147.4, 147.2, 126.3, 124.1, 84.2, 77.8, 77.5, 61.0, 60.9, 60.2, 60.1, 37.8, 35.2, 25.8, 18.1, 14.3, 9.3, 6.8, -4.1, -4.8; IR (film) ν_{max} 2936, 2857, 1737, 1464, 1259, 1077 cm^{-1} ; HRMS(CI, NH_3) m/z calc'd for $\text{C}_{25}\text{H}_{42}\text{O}_7\text{Si}$ $[\text{M}+\text{H}]^+$ 482.6898, found: 482.4878; $[\alpha]_{\text{D}}^{20} +10.53$ (c 1.30, CHCl_3).