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Stereoselective synthesis of the C1-C22 carbon framework of (-)-amphidinolide K

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Abstract: Two stereoselective routes to the C7-C22 subunit of amphidinolide K are disclosed. Jacobsen's hydrolytic kinetic resolution and Sharpless' asymmetric dihydroxylation reactions have been employed for the construction of the THF ring. The C10-C11, C16-C17, C9-O and C18-O bonds have been created using α-chloro sulfide intermediates and [2,3] sigmatropic rearrangement. Marshall's propargylation protocol is utilized to create the C4 stereogenic center and regioselective hydrozirconation/iodine quench afforded an alkenyl iodide which is employed in the NHK coupling with the C7-C22 subunit. Oxonia-Cope rearrangement resulted in the creation of the C18 carbinol stereogenic center and chain elongation.

Introduction

Amphidinolide K (**1**, Figure 1) is a cytotoxic 19-membered macrolide isolated by Kobayashi and co-workers from the cultured dinoflagellate *Amphidinium sp*.[1] It displays cytotoxic activity against murine lymphoma L1210 (IC_{50} = 1.6 μg mL^{-1}) and epidermoic carcinoma KB cells (IC_{50} = 2.9 μg mL^{-1}) in vitro.[2] While amphidinolide H, a 26-membered macrolide stabilizes actin filaments (F-actin)[3] and amphidinolide X, a 16-membered macrolide acts as a globulin actin (G-actin) assembly inhibitor,[4] the biological target of the common amphidinolides of intermediate ring sizes is not known. Williams and co-workers assigned the relative and absolute stereochemistry of the natural product in the first report on

the total synthesis of (+)-amphidinolide K. The groups of Lee[5] and Villarasa[6] reported the synthesis of (-)-amphidinolide K.

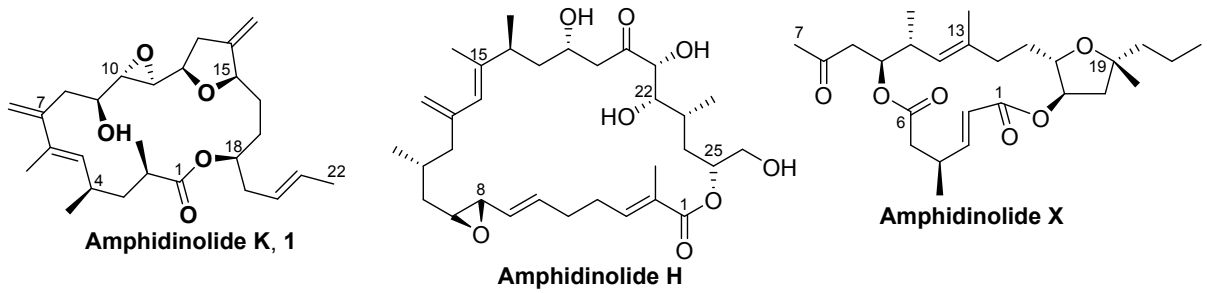
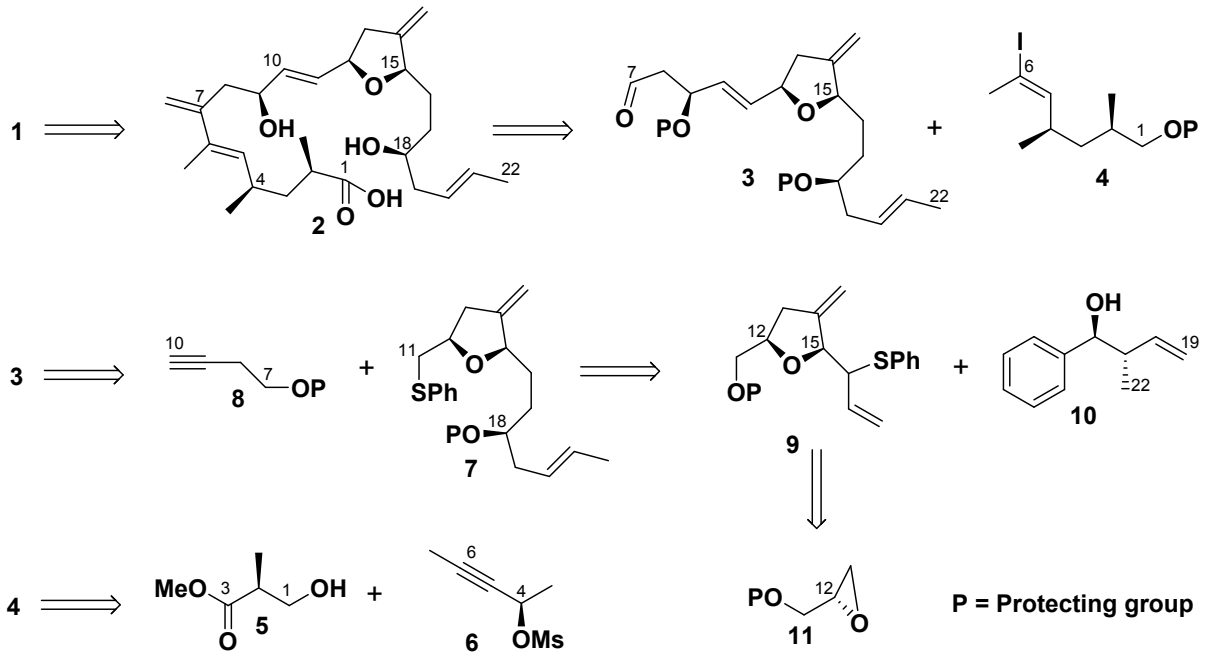


Figure 1. Structures of Amphidinolides K, H and X.

The unique structure and potent bioactivity of amphidinolide has elicited considerable interest and many reports detailing the synthesis of subunits have been published.[7] We disclose herein a convergent stereocontrolled synthesis of the entire carbon framework of amphidinolide K taking advantage of Marshall's propargylation for C3-C4, NHK coupling for C6-C7, α-chloro sulfide intermediates for forging the C10-C11 and C16-C17 bonds and oxonia-Cope rearrangement for C18-C19 bond formation.

Results and discussion

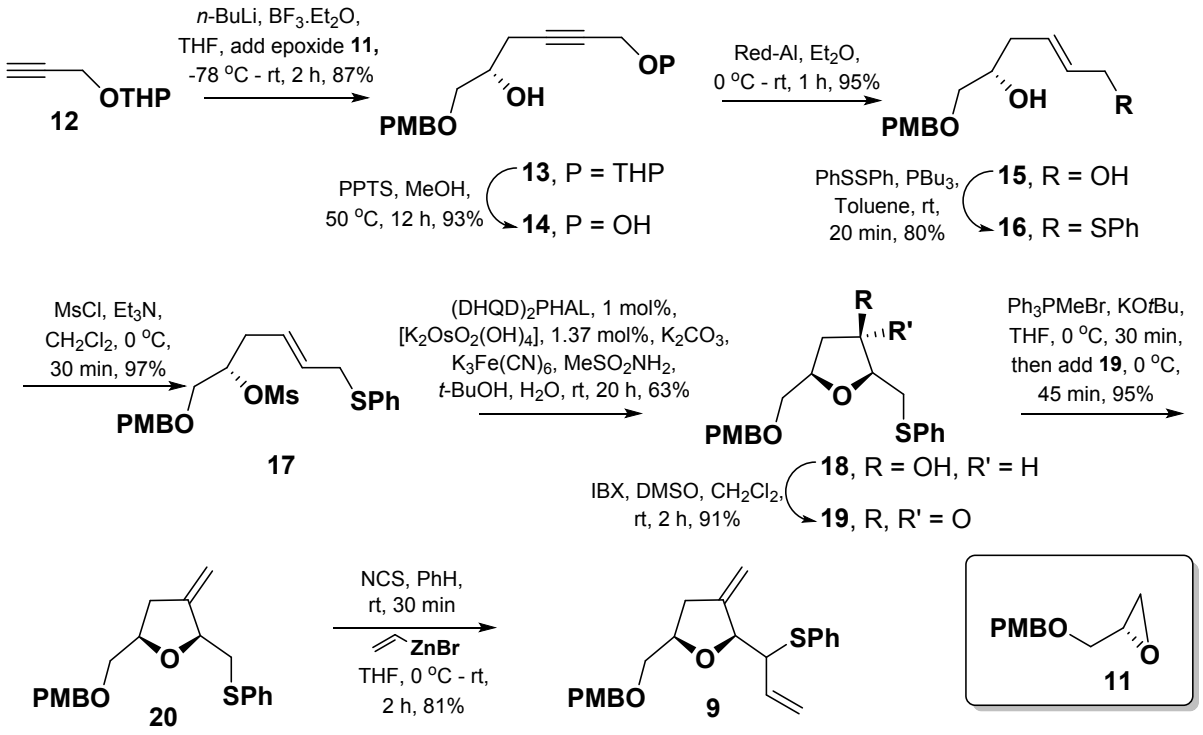
The retrosynthetic disconnection is depicted in Scheme 1. Shina macrolactonization of the hydroxy acid **2** followed by epoxidation would afford amphidinolide K. The hydroxy acid **2** was envisaged to be obtained by NHK-coupling of iodo alkene **4** with aldehyde **3**. Iodo alkene **4** was traced to Roche ester **5** and mesylate **6**. Aldehyde **3** was imagined to be obtained from the reaction of an alkynylzinc bromide derived from alkyne **8** with the α-chloro sulfide, obtained from sulfide **7**, followed by [2,3] sigmatropic rearrangement of the corresponding sulfoxide and further reduction of the ensuing ketone. Sulfide **7** was envisioned to be obtained from the reaction of an aldehyde derived from sulfide **9** with the homoallyl alcohol **10** by utilizing the oxonia-Cope rearrangement. Sulfide **9** can be traced to glycidol ether **11**.



Scheme 1. Retrosynthetic disconnection of amphidinolide K.

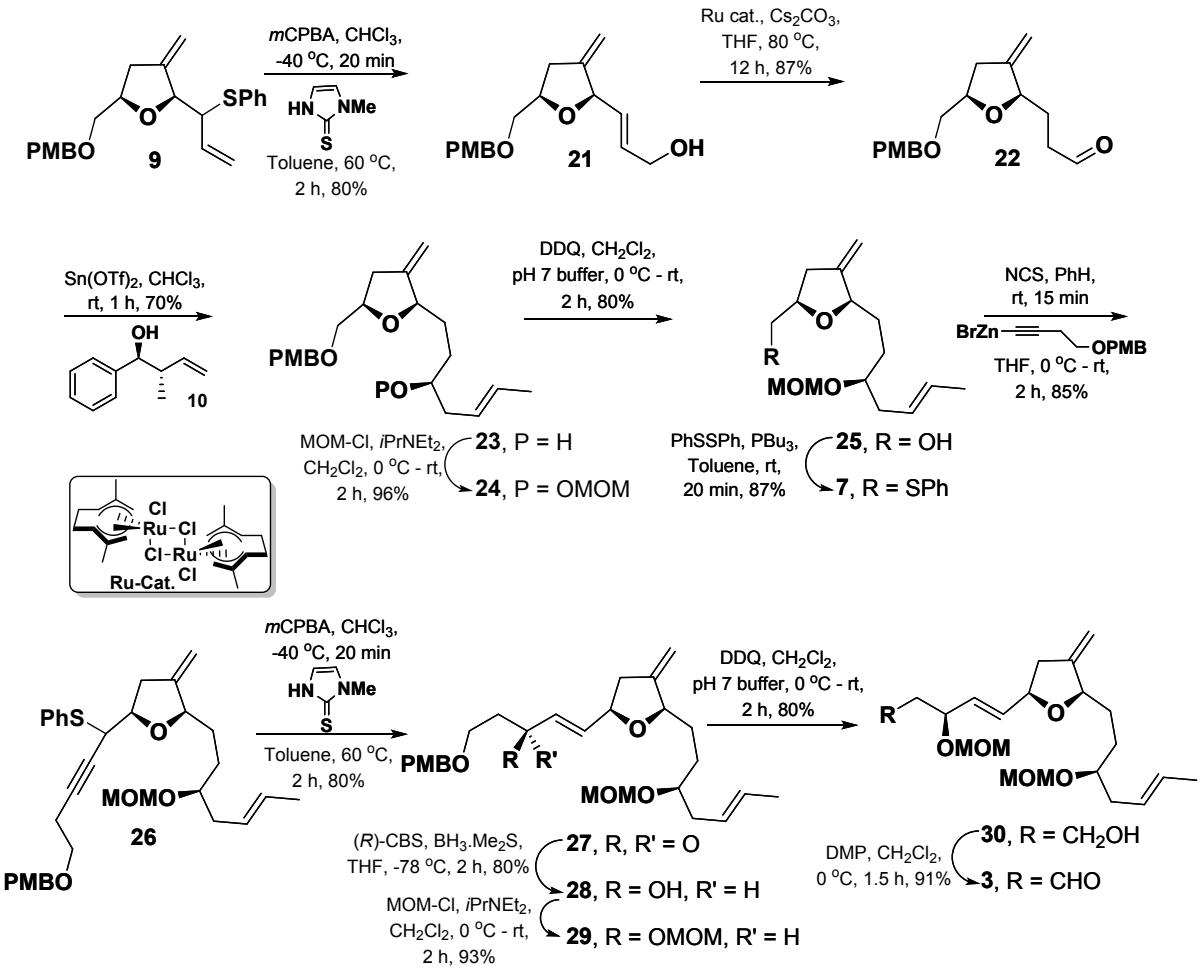
The synthesis of sulfide **7** began from the known epoxide **11**,[8] Scheme 2, obtained by Jacobsen's hydrolytic kinetic resolution, which on reaction with alkyne **12** following Yamaguchi's protocol[9a] yielded alkyne **13**. Deprotection of the hydroxyl by cleavage of the THP ether followed by reduction of the triple bond of the resulting propargylic alcohol **14**, employing Red-Al, afforded allyl alcohol **15**. The sulfide **16**, obtained cleanly using Hata's protocol,[10] was converted to the mesylate **17**. Subjecting mesylate **17** to Sharpless' asymmetric dihydroxylation[11] conditions using $(DHQD)_2PHAL$ ligand afforded the THF derivative **18** via dihydroxylation (dr 7:3) followed by intramolecular displacement.[12] Oxidation of the secondary hydroxyl to ketone **19** using IBX[13] followed by Wittig olefination furnished sulfide **20**. Treatment of sulfide **20** with NCS afforded a chloro sulfide intermediate which on reaction with vinylzinc bromide yielded allyl sulfide **9**.[14] The configuration at C16 was inconsequential since it was to be destroyed subsequently. Oxidation of the sulfide to sulfoxide followed by Mislow-Evans rearrangement[15] furnished the allyl alcohol **21**, Scheme 3, which was subjected to a redox reaction under Ru(IV) catalysis[16] to yield aldehyde **22**.

Aldehyde **22** and the known homoallylic alcohol **10** underwent oxonia-Cope rearrangement[17] in the presence of $Sn(OTf)_2$[18] to yield the homoallyl alcohol **23** (dr >95: <5, 70%).[9b] Protection of the hydroxyl group under standard conditions afforded the MOM-ether **24**.



Scheme 2. Synthesis of sulfide **9**.

Proceeding ahead, the alcohol was deprotected by cleavage of the PMB ether using DDQ[19] to furnish the compound **25**. The sulfide **7** was obtained from alcohol **25** without incident following Hata's protocol. The C10-C11 and the C9-O bonds were envisioned to be created using an α-chloro sulfide intermediate. Thus reaction of chloro sulfide obtained from sulfide **7** with the alkynylzinc bromide prepared from homopropargylic ether **8** furnished the propargylic sulfide **26**.[14] Oxidation followed by [2,3] sigmatropic rearrangement[20] afforded unsaturated ketone **27** which on reduction using (*R*)-CBS reagent[21] yielded alcohol **28**.[9b] Protection of the alcohol as its MOM-ether afforded the compound **29**. Deprotection of the hydroxyl by removal of the PMB ether using DDQ furnished the alcohol **30** which on oxidation using DMP[22] yielded aldehyde **3**, constituting the C7-C22 subunit.

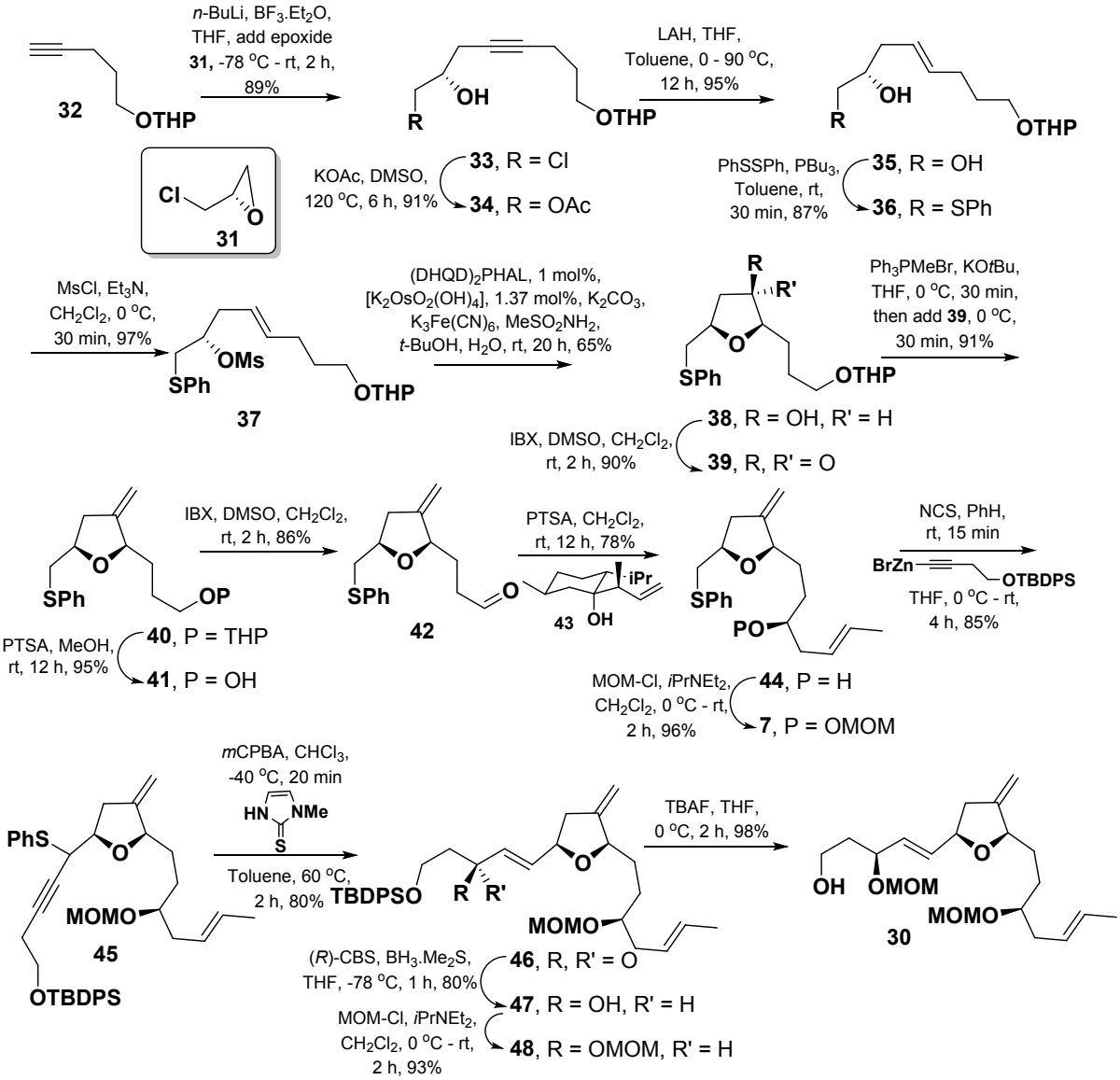


Scheme 3. Synthesis of the C7-C22 subunit.

Alternate shorter route to aldehyde 3

It was reasoned that if the THF subunit corresponding to aldehyde **22** constituting the C11-C18 fragment could be prepared with the C11 atom decorated with the sulfide, the synthetic steps, required for elaboration from an epoxide, similar to **11**, to sulfide **7** could be reduced. Towards this objective an alternate route was designed as depicted in Scheme 4. The synthesis began with (*S*)-epichlorohydrin **31**,[8] which on reaction[9a] with the lithium acetylide derived from pentynol ether **32** afforded chlorohydrin **33**. Nucleophilic displacement of chlorine by an acetate using KOAc in DMSO yielded primary acetate **34** along with a small quantity of the secondary acetate. Treatment of the mixture of acetates with LAH furnished the homoallyl alcohol **35** by deprotection and reduction of the triple bond. The primary

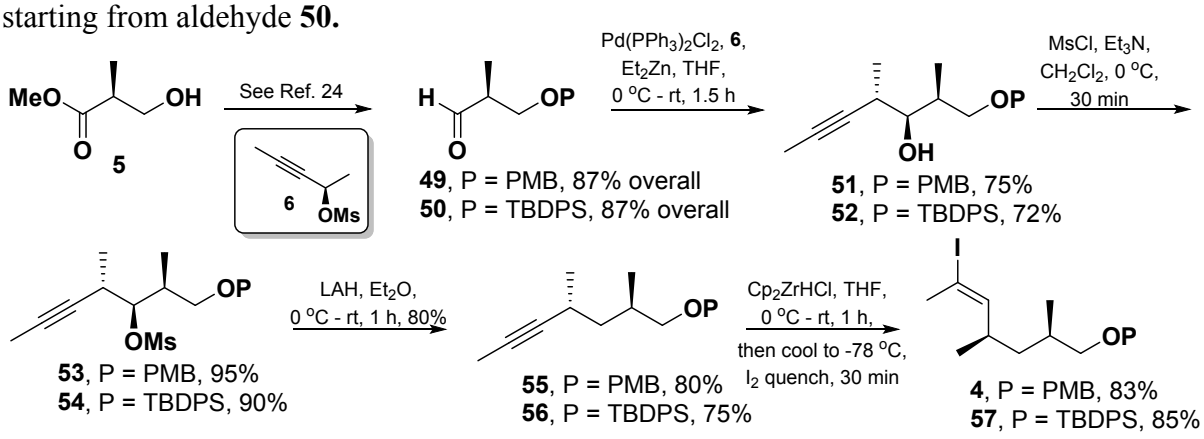
hydroxyl was selectively converted to the sulfide **36**[9b] and the secondary hydroxyl was converted to the mesylate **37**. Sharpless' asymmetric dihydroxylation (dr 7:3) using $(DHQD)_2PHAL$ ligand afforded the THF derivative **38**.[23] Oxidation of the alcohol to the ketone **39** and Wittig olefination furnished exocyclic alkene **40**. Deprotection of the hydroxyl group by cleavage of the THP ether and oxidation of the resulting alcohol **41** yielded aldehyde **42**. Oxonia-Cope rearrangement using the homoallylic alcohol **43** derived from (+)-menthol[17] yielded the alcohol **44**[9b] which on protection using MOM-Cl furnished compound **7**.



Scheme 4. Alternate route to alcohol **30**.

Reaction of the chloro sulfide derived from sulfide **7** with the alkynylzinc bromide obtained from the homopropargyl alcohol protected as its silyl ether furnished sulfide **45** which was subjected to the same two-step one-pot procedure as shown in Scheme 3 (**26** to **27**) to yield ketone **46**. Stereoselective reduction to alcohol **47**[9b] and protection furnished compound **48**. The silyl ether was deprotected in nearly quantitative yield to furnish alcohol **30**, Scheme 4.

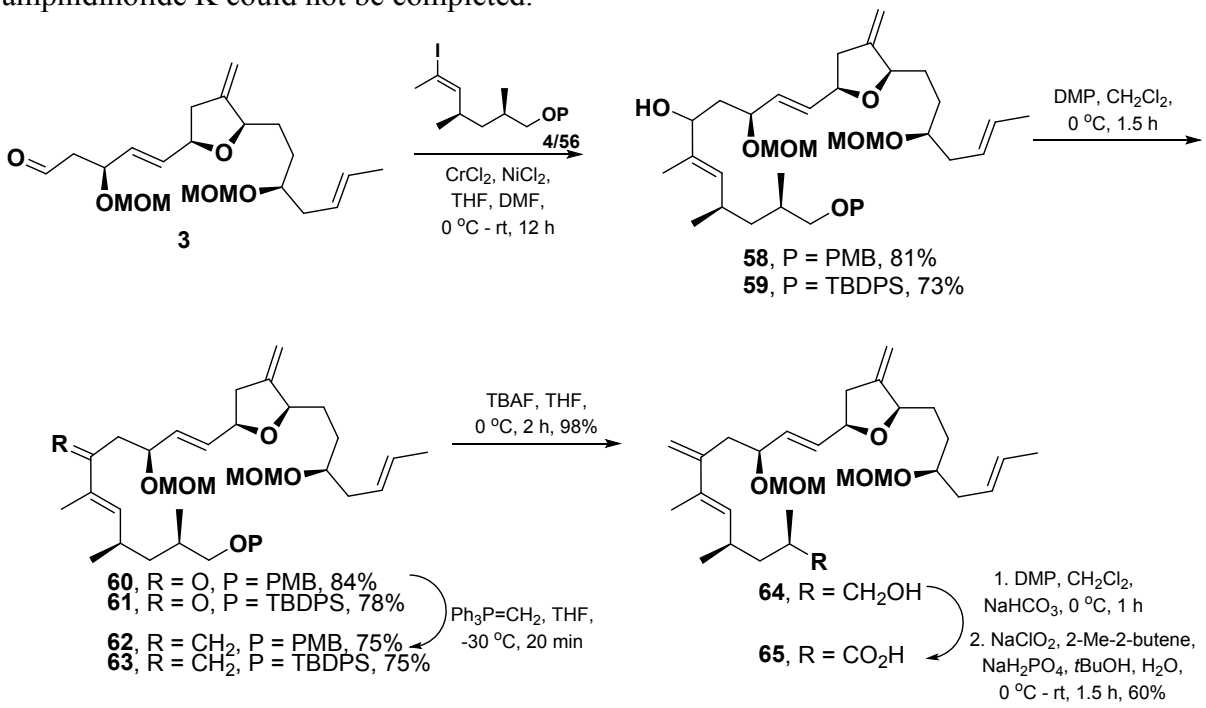
The synthesis of iodo alkene **4** began from Roche ester **5** which was converted by a known sequence of reactions[24] into aldehydes **49** and **50**. Reaction of aldehyde **49**, Scheme 5, with mesylate **6** following Marshall's protocol[25] afforded alkyne **51**. Deoxygenation of the mesylate **53** using LAH afforded alkyne **55** which on hydrozirconation[26] followed by iodine quench yielded iodo alkene **4**. An identical sequence of reactions afforded iodo alkene **57** starting from aldehyde **50.**



Scheme 5. Synthesis of iodo alkenes **4** and **56**.

The union of iodo alkene **4** with aldehyde **3** adopting NHK-coupling conditions[27] afforded an inseparable epimeric mixture of alcohols **58**. Oxidation using DMP furnished the ketone **60** which on subjecting to Wittig olefination afforded alkene **62**. The stage was set for macrolactonization. Towards this end, attempted deprotection of the alcohol by removal of the PMB ether using DDQ furnished a complex mixture of products probably arising from allylic oxidation of the conjugated diene. We were therefore compelled to prepare iodo alkene **57**. The epimeric mixture of alcohols **59**, Scheme 6, resulting from the NHK coupling of aldehyde **3** and iodo alkene **57** was elaborated by the same sequence of reactions to yield

compound **63**. Deprotection of the hydroxyl group by cleavage of the silyl ether proceeded without incident using TBAF to furnish the primary alcohol **64**. Oxidation using DMP followed by Pinnick oxidation[28] of the ensuing aldehyde afforded acid **65**. It only remained to deprotect the alcohol by removal of the MOM ether to effect the macrolactonization. Disappointingly, attempted deprotection using TMS-Br[29] or $ZnBr_2$ in the presence of butane thiol[30] afforded a complex mixture of products. At this stage we ran out of sample to attempt the deprotection of the MOM-ether under different conditions and therefore the synthesis of amphidinolide K could not be completed.



Scheme 6. Synthesis of acid **65** constituting the entire carbon framework of amphidinolide K.

Conclusion

Stereoselective routes to the C7-C22 subunit of amphidinolide K are disclosed. The C10-C11, C16-C17, C18-O and C9-O bonds are created using α-chloro sulfide intermediates. The C1-C6 subunit was synthesized using Marshall's propargylation as the key step. NHK-coupling was employed for coupling the C1-C6 with C7-C22 subunit. Oxonia-Cope rearrangement, [2,3] sigmatropic rearrangement, Ru(IV)-catalyzed redox rearrangement, Jacobsen's hydrolytic kinetic resolution and Sharpless' asymmetric dihydroxylation with

concomitant cyclization constitute the unique features of the synthesis. The potential of α-chloro sulfides for stereoselective carbon-carbon bond formation is elegantly demonstrated.

Experimental

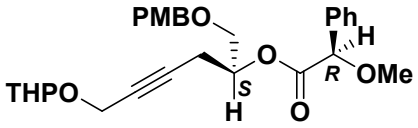
(*S*)-2-(((4-Methoxybenzyl)oxy)methyl)oxirane 11[31]**:** The catalyst (*R*,*R*)-salen-Co(II) (454 mg, 0.75 mmol) was dissolved in dichloromethane (5 mL) and treated with acetic acid (285 µL, 5 mmol). The solution was allowed to stir at rt in open air for 30 min over which time the color changed from orange-red to dark brown. The solution was concentrated in vacuo to yield a crude brown solid, which was dissolved in THF (2.5 mL) and then racemic epoxide (29.1 g, 150 mmol) was added to the solution. The reaction mixture was cooled at 0 °C and H_2O (1.5 mL, 82.5 mmol) was added dropwise over a 5 min period. The reaction mixture was allowed to warm to rt and stirred for 12 h. Direct purification by flash chromatography on silica gel using 5% EtOAc/hexane as the eluent provided the enantioenriched epoxide **11** (7.66 g, 63 mmol) in 42% yield as a colourless oil. TLC: R_f 0.3 (10% EtOAc/Hexane); $[\alpha]^{20}_D$ -3.5 (*c* 1.0, $CHCl_3$); IR (Neat) 2925, 2856, 1727, 1085, 994, 810 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.27 (d, *J* = 8.6 Hz, 2H), 6.88 (d, *J* = 8.6 Hz, 2H), 4.54 (d, *J* = 11.5 Hz, 1H), 4.48 (d, *J* = 11.5 Hz, 1H), 3.80 (s, 3H), 3.72 (dd, *J* = 11.4, 3.1 Hz, 1H), 3.41 (dd, *J* = 11.4, 5.8 Hz, 1H), 3.19 – 3.15 (m, 1H), 2.81 – 2.76 (m, 1H), 2.60 (dd, *J* = 5.0, 2.7 Hz, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 159.3, 130.0, 129.5, 113.8, 73.0, 70.6, 55.3, 50.9, 44.4; MS (ESI-TOF) *m/z*: 217 [M+Na]+. HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ calcd for $C_{11}H_{14}O_3Na$: 217.0841; found: 217.0848.

(2*S*)-1-((4-Methoxybenzyl)oxy)-6-((tetrahydro-2H-pyran-2-yl)oxy)hex-4-yn-2-ol 13: To a stirred solution of alkyne **12** (9.1 g, 65 mmol) in anhydrous THF (150 mL) was added *n*-BuLi (2.5 M in THF, 26 mL, 65 mmol) under N_2 at -78 ºC. After 30 min the solution of the epoxide **11** (9.7 g, 50 mmol) in anhydrous THF (50 mL) was added over a period of 15 minutes, followed by $BF_3.Et_2O$ (10.4 mL, 84 mmol). The mixture was stirred at -78 °C for 1 h

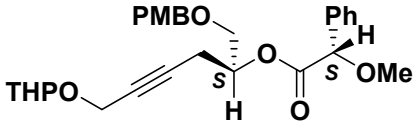
and was allowed to warm to rt over period of 1 h. The reaction mixture was cooled to 0 °C and quenched with satd aq NH_4Cl (100 ml). The layers were separated and the aq layer extracted with EtOAc (3x100mL). The combined organic layers were washed with water (100 mL), brine (100 mL), dried over Na_2SO_4 and concentrated. The residue was purified by column chromatography using 10% EtOAc/Hexane (v/v) to afford the alcohol **13** (14.52 g, 43.5 mmol) in 87% yield as a colourless liquid. TLC: R_f 0.2 (10%EtOAc/Hexane); $[\alpha]^{20}_D$ -1.6 (*c* 1, $CHCl_3$); IR (Neat) 3421, 2941, 2866, 1607, 1513, 1251, 1115, 1024, 816, 771 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.26 (d, *J* = 8.4 Hz, 2H), 6.88 (d, *J* = 8.6 Hz, 2H), 4.78 (t, *J* = 3.3 Hz, 1H), 4.49 (s, 2H), 4.32 – 4.16 (m, 2H), 3.97 – 3.91 (m, 1H), 3.88 – 3.82 (m, 1H), 3.81 (s, 3H), 3.57 (dd, *J* = 9.6, 3.9 Hz, 1H), 3.54 – 3.49 (m, 1H), 3.46 (dd, *J* = 9.5, 6.6 Hz, 1H), 2.61 (s, 1H), 2.52 – 2.44 (m, 2H), 1.89 – 1.69 (m, 3H), 1.66 – 1.50 (m, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 159.3, 129.9, 129.4, 113.8, 96.8, 82.2, 78.2, 73.1, 72.6, 68.9, 62.0, 55.2, 54.6, 30.2, 25.3, 23.9, 19.1; MS (ESI-TOF) *m/z*: 357 $[M+Na]^+$. HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ calcd for $C_{19}H_{26}O_5Na$: 357.1688; found: 357.1672.

General procedure for the preparation of mandelate ester:

To a solution of the alcohol (30 μmol, 1 eq) in dichloromethane (0.5 mL) cooled at 0 °C was added (*R*)-methoxyphenylacetic acid (39 μmol, 1.3 eq), DMAP (1 mg, 20 mol%) and EDC.HCl (45 μmol, 1.5 eq). The reaction mixture was stirred at rt for 2 h. After complete consumption of starting material, the reaction mixture was diluted with dichloromethane (2 mL) and H_2O (2 mL). The layers were separated and the aq layer was extracted with dichloromethane (2x5 mL). The combined organic layers were sequentially washed with satd aq $NaHCO_3$ (5 mL), 1N HCl (5 mL), H_2O (2x5 mL), brine (10 mL), dried over Na_2SO_4 and concentrated under reduced pressure to afford the ester.



(2*R*)-(2*S*)-1-((4-methoxybenzyl)oxy)-6-((tetrahydro-2H-pyran-2-yl)oxy)hex-4-yn-2-yl 2-methoxy-2-phenylacetate I: Following the general procedure, alcohol **13** (17 mg, 50 μmol) on reaction with (*R*)-methoxyphenylacetic acid (11 mg, 65 μmol) afforded ester **I** (23 mg, , 47 μmol) in 95% yield as a liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48 – 7.42 (m, 2H), 7.37 – 7.31 (m, 3H), 7.22 (d, *J* = 8.7 Hz, 2H), 6.87 (d, *J* = 8.7 Hz, 2H), 5.18 – 5.09 (m, 1H), 4.78 (s, 1H), 4.72 (dd, *J* = 6.5, 3.3 Hz, 1H), 4.48 (d, *J* = 11.6 Hz, 1H), 4.42 (d, *J* = 11.6 Hz, 1H), 4.12 (dt, *J* = 15.4, 2.0 Hz, 1H), 4.04 (dt, *J* = 15.4, 2.0 Hz, 1H), 3.85 – 3.77 (m, 4H), 3.62 (d, *J* = 4.9 Hz, 2H), 3.55 – 3.47 (m, 1H), 3.42 (s, 3H), 2.55 – 2.40 (m, 2H), 1.84 – 1.49 (m, 6H).



(2*S*)-(2*S*)-1-((4-methoxybenzyl)oxy)-6-((tetrahydro-2H-pyran-2-yl)oxy)hex-4-yn-2-yl 2-methoxy-2-phenylacetate II: Following the general procedure, alcohol **13** (17 mg, 50 μmol) on reaction with (*S*)-methoxyphenylacetic acid (11 mg, 65 μmol) afforded ester **II** (23 mg, 47 μmol) in 94% yield as a liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50 – 7.41 (m, 2H), 7.36 – 7.30 (m, 3H), 7.09 (d, *J*= 8.7 Hz, 2H), 6.83 (d, *J* = 8.7 Hz, 2H), 5.20 – 5.11 (m, 1H), 4.80 (s, 1H), 4.77 (t, *J* = 3.3 Hz, 1H), 4.29 (d, *J* = 11.6 Hz, 1H), 4.26 – 4.11 (m, 3H), 3.87 – 3.81 (m, 1H), 3.80 (s, 3H), 3.55 – 3.44 (m, 3H), 3.42 (s, 3H), 2.70 – 2.52 (m, 2H), 1.86 – 1.50 (m, 6H).

Note: The configuration of alcohol **13** was unambiguously established as '*S*' by comparison of the ^{1}H NMR spectra of both (*R*) & (*S*)-mandelate esters. Thus the propargylic protons appeared upfield in the *R*-mandelate compared to the *S*-mandelate while the CH_2OPMB appeared downfield in the *R*-mandelate ester compared to the *S*-diastereomer.

(*S*)-6-((4-Methoxybenzyl)oxy)hex-2-yne-1,5-diol 14: To solution of alkyne **13** (14 g, 42 mmol) in methanol (42 mL) was added PPTS (105 mg, 1 mol%) and the mixture stirred at 50 ^{o}C for 12 h. The solvent was evaporated and the residue was dissolved in ethyl acetate (100 mL) and washed with satd aq $NaHCO_3$ (50 mL), water (50 mL), brine (50 mL) and dried over anhydrous Na_2SO_4. After filtration, the solvent was evaporated under reduced pressure and the crude product was purified by flash column chromatography using 10-20% EtOAc/Hexane (v/v) as the eluent to afford the primary alcohol **14** (9.76 g, 39.1 mmol) in 93% yield as a colorless oil. TLC: R_f 0.2 (30% EtOAc/Hexane); $[\alpha]^{20}_D$ +7.1 (*c* 1.1, $CHCl_3$); IR (Neat) 3388, 2912, 2864, 1612, 1513, 1247, 1100, 1030, 820 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.25 (d, *J* = 8.3 Hz, 2H), 6.88 (d, *J* = 8.7 Hz, 2H), 4.48 (s, 2H), 4.21 (t, *J* = 2.2 Hz, 2H), 3.98 – 3.90 (m, 1H), 3.80 (s, 3H), 3.54 (dd, *J* = 9.6, 4.0 Hz, 1H), 3.45 (dd, *J* = 9.6, 6.6 Hz, 1H), 2.45 (dt, *J* = 6.1, 2.2 Hz, 2H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 159.2, 129.7, 129.4, 113.7, 81.8, 80.7, 73.0, 72.6, 68.7, 55.2, 50.8, 23.8; MS (ESI-TOF) *m/z*: 273 $[M+Na]^+$. HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ calcd for $C_{14}H_{18}O_4Na$: 273.1112; found: 273.1103.

(*S*,*E*)-6-((4-Methoxybenzyl)oxy)hex-2-ene-1,5-diol 15: The solution of alkyne **14** (9.5 g, 38 mmol) in anhydrous Et_2O (40 mL) was added dropwise to sodium bis-(2-methoxyethoxy)aluminium hydride (60 wt% in toluene, 35 mL, 116 mmol) in anhydrous Et_2O (40 mL) maintained at 0 ^{o}C in a rb flask. The reaction mixture was gradually warmed to rt, stirred at the same temperature for 1 h and then cooled to 0 ^{o}C. The reaction mixture was quenched with aq 1M HCl solution (40 mL). The layers were separated and the aq layer was extracted with Et_2O (3x80 mL). The combined organic layers were dried over Na_2SO_4 and concentrated. The residue was purified by column chromatography using 20-30% EtOAc/Hexane (v/v) as the eluent to give pure compound **15** (9.1 g, 36.1 mmol) in 95% yield as a colourless liquid. TLC: R_f 0.2 (40% EtOAc/Hexane); $[\alpha]^{20}_D$ +1.4 (*c* 0.95, $CHCl_3$); IR (Neat) 3421, 2931, 2863, 1612, 1513, 1247, 1090, 1032, 819, 771 cm^{-1}; ^{1}H NMR (500 MHz,

$CDCl_3$) δ 7.25 (d, *J* = 8.6 Hz, 2H), 6.88 (d, *J* = 8.6 Hz, 2H), 5.79 – 5.61 (m, 2H), 4.47 (s, 2H), 4.07 (d, *J* = 4.3 Hz, 2H), 3.90 – 3.82 (m, 1H), 3.81 (s, 3H), 3.46 (dd, *J* = 9.5, 3.4 Hz, 1H), 3.33 (dd, *J* = 9.5, 7.4 Hz, 1H), 2.28 – 2.15 (m, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 159.2, 132.1, 129.9, 129.4, 128.0, 113.8, 73.6, 72.9, 69.7, 63.1, 55.2, 36.1; MS (ESI-TOF) *m/z*: 275 $[M+Na]^+$. HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ calcd for $C_{14}H_{20}O_4Na$: 275.1250; found: 275.1254.

(*S*,*E*)-1-((4-Methoxybenzyl)oxy)-6-(phenylthio)hex-4-en-2-ol 16: To a solution of alcohol **15** (8.32 g, 33 mmol) in toluene (57 mL) at rt was added diphenyl disulfide (7.91 g, 36.3 mmol) followed by tri-*n*-butylphosphine (16.3 mL, 66 mmol). The reaction mixture was stirred at ambient temperature for 20 min. The solvent was removed under reduced pressure and the residue was purified by flash column chromatography on silica gel using 10% EtOAc/Hexane (v/v) as the eluent to afford sulfide **16** as colorless oil (9.87 g, 28.7 mmol) in 87% yield. TLC: R_f 0.3 (10% EtOAc/Hexane); $[\alpha]^{20}_D$ +8.0 (*c* 0.75, $CHCl_3$): IR (Neat) 3450, 2907, 2859, 1611, 1511, 1246, 1089, 1031, 967, 819, 741, 691 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.34 – 7.31 (m, 2H), 7.28 – 7.25 (m, 2H), 7.24 (d, *J*= 8.7 Hz, 2H), 7.21 – 7.15 (m, 1H), 6.88 (d, *J* = 8.7 Hz, 2H), 5.61 – 5.45 (m, 2H), 4.43 (s, 2H), 3.81 (s, 3H), 3.75 – 3.68 (m, 1H), 3.55 – 3.49 (m, 2H), 3.34 (dd, *J* = 9.5, 3.5 Hz, 1H), 3.22 (dd, *J* = 9.5, 7.2 Hz, 1H), 2.17 (t, *J* = 6.3 Hz, 2H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 159.2, 135.7, 130.1, 130.0, 129.33, 129.25, 128.7, 128.3, 126.2, 113.8, 73.3, 72.9, 69.7, 55.2, 36.3; MS (ESI-TOF) *m/z*: 367 $[M+Na]^+$. HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ calcd for $C_{20}H_{24}O_3NaS$: 367.1338; found: 367.1349.

(*S*,*E*)-1-((4-Methoxybenzyl)oxy)-6-(phenylthio)hex-4-en-2-yl methanesulfonate 17: Triethylamine (8.6 mL, 61.6 mmol) and methanesulfonyl chloride (2.6 mL, 33.6 mmol) were added successively to a solution of alcohol **16** (9.63 g, 28 mmol) in anhydrous CH_2Cl_2 (56 mL) at 0 °C. The reaction mixture was stirred at 0 °C for 30 min before it was quenched by

the addition of satd aq $NaHCO_3$ (50 mL) at 0 °C. After the mixture was warmed to 25 °C, the organic layer was separated and the aq layer was extracted with CH_2Cl_2 (2x70 mL). The combined organic extracts were washed with water (100 mL), brine (100 mL), dried over Na_2SO_4, filtered and concentrated to afford mesylate **17** (11.46 g, 27.16 mmol) in 97% yield as a pale yellow oil, which was used in the next step without further purification. TLC: R_f 0.3 (10% EtOAc/Hexane); $[\alpha]^{20}_D$ +14.2 (*c* 1, $CHCl_3$); IR (Neat) 2935, 2866, 1612, 1513, 1248, 1174, 1095, 917, 818, 743 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.33 – 7.29 (m, 2H), 7.27 (m, 2H), 7.21 (d, *J* = 8.7 Hz, 2H), 7.20 – 7.16 (m, 1H), 6.87 (d, *J* = 8.7 Hz, 2H), 5.62 (dt, *J* = 15.2, 6.8 Hz, 1H), 5.49 (dt, *J* = 15.2, 7.1 Hz, 1H), 4.74 – 4.65 (m, 1H), 4.42 (d, *J* = 11.4 Hz, 1H), 4.37 (d, *J* = 11.4 Hz, 1H), 3.80 (s, 3H), 3.51 (d, *J* = 6.9 Hz, 2H), 3.43 (d, *J* = 5.2 Hz, 2H), 2.95 (s, 3H), 2.47 – 2.36 (m, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 159.3, 135.6, 129.9, 129.7, 129.4, 129.3, 128.8, 126.7, 126.2, 113.8, 80.9, 72.9, 70.3, 55.2, 38.5, 35.9, 34.8; MS (ESI-TOF) *m/z*: 445 $[M+Na]^+$. HRMS (ESI-TOF) *m/z*: $[M+H]^+$ calcd for $C_{21}H_{27}O_5S_2$: 423.1294; found: 423.1306.

(2*S*,3*R*,5*R*)-5-(((4-Methoxybenzyl)oxy)methyl)-2-((phenylthio)methyl)tetrahydrofuran-3-ol 18: To a stirred solution of K_2CO_3 (11.2 g, 81 mmol), $K_3[Fe(CN)_6]$ (26.5 g, 81 mmol) and hydroquinine 1,4-phthalazinediyl diether [$(DHQD)_2PHAL$, 110 mg, 0.14 mmol] in *t*BuOH/H_2O (100 mL, 1:1) were added methane sulfonamide (2.6 g, 27 mmol) and $K_2OsO_2(OH)_4$ (10 mg, 0.027 mmol) at rt and the solution was stirred for 15 min. The reaction mixture was cooled to 0 °C and a solution of mesylate **17** (11.4 g, 27 mmol) in *t*BuOH/H_2O (35 mL, 1:1) was added. The resultant mixture was stirred at the same temperature for 10 h. The reaction mixture was then warmed to rt and stirred for 10 h. Upon completion (monitored by TLC), the reaction mixture was quenched with a satd solution of Na_2SO_3 (80 mL). The aq layer was separated and then extracted with EtOAc (3x100 mL). The combined organic extracts were washed with brine, dried with anhydrous Na_2SO_4 and concentrated under

reduced pressure. The crude residue was purified by silica gel column chromatography using 10% EtOAc/Hexane (v/v) as the eluent to give tetrahydrofuran derivative **18** (6.12 g, 17.0 mmol) in 63% yield as a viscous liquid; TLC: R_f 0.2 (10% EtOAc/Hexane); $[\alpha]^{20}_D$ -30.1 (*c* 1.5, $CHCl_3$); IR (Neat) 3436, 2925, 1612, 1512, 1246, 1175, 1076, 1033, 820, 744 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.39 – 7.35 (m, 2H), 7.30 – 7.23 (m, 4H), 7.19 – 7.12 (m, 1H), 6.88 (d, *J* = 8.7 Hz, 2H), 4.61 (d, *J* = 11.5 Hz, 1H), 4.47 (d, *J* = 11.5 Hz, 1H), 4.25 (dq, *J* = 10.3, 2.0 Hz, 1H), 4.10 (bs, 1H), 4.06 – 3.96 (m, 1H), 3.82 (td, *J* = 6.6, 2.4 Hz, 1H), 3.79 (s, 3H), 3.69 (dd, *J* = 10.3, 2.0 Hz, 1H), 3.38 (dd, *J* = 10.3, 2.0 Hz, 1H), 3.25 (dd, *J* = 13.3, 6.7 Hz, 1H), 3.19 (dd, *J* = 13.3, 6.6 Hz, 1H), 2.31 (ddd, *J* = 14.1, 10.4, 5.1 Hz, 1H), 1.94 (dd, *J* = 14.1, 2.7 Hz, 1H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 159.4, 136.5, 129.5, 129.0, 128.8, 128.7, 125.7, 113.8, 82.7, 76.7, 73.3, 71.3, 71.1, 55.1, 36.9, 32.2; MS (ESI-TOF) *m/z*: 383 $[M+Na]^+$. HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{20}H_{24}O_4NaS$: 383.1286; found: 383.1288.

(2*S*,5*R*)-5-(((4-Methoxybenzyl)oxy)methyl)-2- ((phenylthio)methyl)dihydrofuran-3(2H)-one 19: To a stirred solution of 2-iodoxybenzoic acid (7.14 g, 25.5 mmol) in anhydrous DMSO (34 mL) cooled at 0 ^oC was added a solution of alcohol **18** (6.12 g, 17 mmol) in anhydrous dichloromethane (52 mL) and the reaction mixture was stirred for a period of 2 h at rt. After completion of the reaction, the mixture was filtered through a small pad of Celite pad and the filtrate was diluted with CH_2Cl_2 (80 mL), washed with water (200mL), brine (100 mL) and dried over Na_2SO_4. The solvent was evaporated under reduced pressure to afford the residue which was purified by column chromatography using 5% EtOAc/Hexane (v/v) as the eluent to give the pure ketone **19** (5.54 g, 15.47 mmol) in 91% yield as a colourless liquid. TLC: R_f 0.2 (7% EtOAc/Hexane); $[\alpha]^{20}_D$ +116.6 (*c* 1.65, $CHCl_3$); IR (Neat) 2908, 2862, 1758, 1611, 1512, 1247, 1173, 1089, 1031, 820, 743, 693 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.44 – 7.33 (m, 2H), 7.30 – 7.21 (m, 4H), 7.17 (tt, *J* = 8.3, 2.2 Hz, 1H), 6.86

(d, *J* = 8.6 Hz, 2H), 4.48 (s, 2H), 4.45 – 4.35 (m, 1H), 4.07 (dd, *J* = 6.3, 3.6 Hz, 1H), 3.79 (s, 3H), 3.65 (dd, *J* = 10.5, 3.6 Hz, 1H), 3.56 (dd, *J* = 10.5, 4.9 Hz, 1H), 3.38 (dd, *J* = 14.0, 3.6 Hz, 1H), 3.13 (dd, *J* = 14.0, 6.4 Hz, 1H), 2.54 (dd, *J* = 18.2, 6.6 Hz, 1H), 2.44 (dd, *J* = 18.2, 9.0 Hz, 1H); $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$) δ 213.3, 159.2, 135.9, 129.7, 129.5, 129.2, 128.8, 126.2, 113.7, 79.9, 75.2, 73.1, 71.2, 55.1, 39.4, 35.1; MS (ESI-TOF) *m/z*: 381 $[M+Na]^+$. HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{20}H_{22}O_4NaS$: 381.1136; found: 381.1139.

(2*S*,5*R*)-5-(((4-Methoxybenzyl)oxy)methyl)-3-methylene-2-((phenylthio)methyl)tetrahydrofuran 20: Methyltriphenylphosphonium bromide (26.8 g, 75 mmol) was suspended in THF (120 mL) and a solution of potassium *tert*-butoxide solution in THF (8.4 g, 75 mmol) was added dropwise at 0 °C. After addition, the resultant yellow solution was stirred for 45 min and was added to the solution of ketone **19** (5.37 g, 15 mmol) in THF (30 mL) at 0 °C. The reaction mixture was stirred for 45 min and then quenched with H_2O (50 mL). The mixture was extracted with EtOAc (3x100 mL). The combined organic extracts were washed with brine (100 mL), dried over anhydrous Na_2SO_4, filtered, and concentrated. The residue was purified by silica gel column chromatography using 3% EtOAc/Hexanes (v/v) as the eluent to afford the pure compound **20** (5.1 g, 14.25 mmol) in 95% yield as a colourless oil. TLC: R_f 0.3 (5% EtOAc/Hexane); $[\alpha]^{20}_D$ +87.7 (*c* 0.95, $CHCl_3$); IR (Neat) 2903, 2860, 1611, 1512, 1247, 1175, 1087, 1033, 819, 741, 692 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.38 (d, *J* = 7.3 Hz, 2H), 7.30 – 7.22 (m, 4H), 7.15 (t, *J* = 7.3 Hz, 1H), 6.86 (d, *J* = 8.6 Hz, 2H), 5.1 – 4.95 (m, 2H), 4.58 – 4.52 (m, 1H), 4.50 (d, *J* = 11.7 Hz, 1H), 4.46 (d, *J* = 11.7 Hz, 1H), 4.19 – 4.08 (m, 1H), 3.79 (s, 3H), 3.51 (d, *J* = 5.0 Hz, 2H), 3.17 (dd, *J* = 5.5, 1.0 Hz, 2H), 2.60 (dd, *J* = 15.5, 6.1 Hz, 1H), 2.53 – 2.40 (m, 1H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 159.1, 149.5, 136.8, 130.2, 129.3, 129.0, 128.8, 125.8, 113.7, 106.4,

79.5, 77.8, 73.0, 71.9, 55.2, 39.3, 35.9; MS (ESI-TOF) *m/z*: 379 $[M+Na]^+$. HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{21}H_{24}O_3NaS$: 379.1344; found: 379.1341.

(2*S*,5*R*)-5-(((4-Methoxybenzyl)oxy)methyl)-3-methylene-2-(1-(phenylthio)allyl)tetrahydrofuran 9: To a solution vinyl magnesium bromide (1M in THF, 36 mL, 36 mmol) cooled at 0 °C was added a solution of $ZnBr_2$ (1.5 M in THF, 36 mL, 54 mmol) at 0 °C and the mixture stirred for 30 min. Separately, in another rb flask, the chloro sulfide was prepared by adding a solution of sulfide **20** (4.27 g, 12 mmol) in anhydrous benzene (60 mL) to NCS (1.67 g, 12.6 mmol) in anhydrous benzene (60 mL) and stirring for 45 min. To the organozinc reagent maintained at 0 °C was added a solution of chloro sulfide (12 mmol) in benzene (120 mL). The reaction mixture was stirred gradually, allowing it to attain rt and stirred further for a period of 2 h when TLC examination indicated complete consumption of the chloro sulfide. The reaction mixture was cooled to 0 °C and quenched by the addition of aq satd NH_4Cl solution (50 mL). It was allowed to warm to rt and diluted with EtOAc (80 mL). The layers were separated and the aq layer was extracted with EtOAc (3x80 mL). The combined organic layers were washed with H_2O (100 mL), brine (100 mL) and dried over anhydrous Na_2SO_4.The solvent was evaporated under reduced pressure to afford a crude compound that was purified by column chromatography using 1−2% EtOAc/hexanes (v/v) as the eluent to afford the pure product **9** (3.66 g, 9.6 mmol) in 81% yield as a light yellow liquid. TLC: R_f 0.3 (5% EtOAc/Hexane); $[\alpha]^{20}_D$ +51.3 (*c* 0.5, $CHCl_3$); IR (Neat) 2903, 2861, 1611, 1512, 1247, 1175, 1088, 1034, 821, 743, 693 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.41 – 7.37 (m, 2H), 7.30 – 7.22 (m, 4H), 7.22 – 7.09 (m, 1H), 6.88 (d, *J* = 8.7 Hz, 2H), 5.9 (ddd, *J* = 17.1, 10.2, 9.0 Hz, 1H), 5.15 – 5.12 (m, 2H), 5.03 (d, *J* =10.2 Hz, 1H), 5.01 (d, *J* = 16.5 Hz, 1H), 4.63 – 4.59 (m, 1H), 4.56 (d, *J* = 11.7 Hz, 1H), 4.53 (d, *J* = 11.7 Hz, 1H), 4.16 – 4.09 (m, 1H), 3.79 (s, 3H), 3.52 (dd, *J* = 10.4, 6.3 Hz, 1H), 3.16 (dd, *J* = 10.4, 4.3 Hz, 1H), 2.60 (dd, *J* = 15.5, 6.1 Hz, 1H), 2.48 – 2.39 (m, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ

159.1, 148.1, 135.6, 135.0, 132.2, 130.3, 129.3, 128.7, 126.9, 117.0, 113.7, 107.0, 82.8, 78.3, 73.0, 71.9, 57.7, 55.2, 37.0; MS (ESI-TOF) *m/z*: 405 $[M+Na]^+$. HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{23}H_{26}O_3NaS$: 405.1500; found: 405.1502.

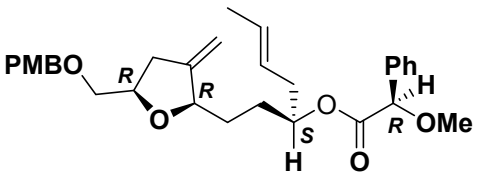
(*E*)-3-((2*R*,5*R*)-5-(((4-Methoxybenzyl)oxy)methyl)-3-methylenetetrahydrofuran-2-yl)prop-2-en-1-ol 21: To a solution of sulfide **9** (3.1 g, 8.1 mmol) in $CHCl_3$ (16 mL) cooled at -40 °C was added *m*CPBA (70%, 2 g, 8.1 mmol) and the reaction mixture stirred at the same temperature for 20 min. Toluene (32 mL) and 2-mercapto-1-methyl-imidazole (1.4 g, 12.2 mmol) were added. The reaction mixture was stirred at 60 °C for 2 h and then quenched by the addition of satd aq $NaHCO_3$ (50 mL). The mixture was diluted with CH_2Cl_2 (50 mL) and the layers were separated. The combined organic layers were washed successively with water (80 mL), brine (50 mL) and dried over Na_2SO_4. The solvent was evaporated under reduced pressure to furnish the crude compound which was purified by column chromatography using 20% EtOAc/hexanes (v/v) as the eluent to afford the product **21** (1.88 g, 6.5 mmol) in 80% yield as a liquid. TLC: R_f0.2 (20% EtOAc/hexanes); $[\alpha]^{20}_D$ +54.7 (*c* 0.5, $CHCl_3$); IR (Neat) 3417, 2924, 2858, 1614, 1512, 1247, 1175, 1094, 1030, 820 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.26 (d, *J* = 8.5 Hz, 2H), 6.87 (d, *J* = 8.6 Hz, 2H), 5.91 (dt, *J* = 15.4, 5.3 Hz, 1H), 5.69 – 5.60 (m, 1H), 5.03 – 4.99 (m, 1H), 4.85 – 4.81 (m, 1H), 4.74 – 4.68 (m, 1H), 4.53 (d, *J* = 11.7 Hz, 1H), 4.48 (d, *J* = 11.7 Hz, 1H), 4.20 – 4.12 (m, 3H), 3.80 (s, 3H), 3.56 – 3.46 (m, 2H), 2.65 (dd, *J* = 16.2, 6.8 Hz, 1H), 2.45 – 2.35 (m, 1H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 159.2, 149.8, 132.6, 130.5, 130.2, 129.4, 113.7, 106.5, 81.9, 77.3, 73.1, 72.0, 62.9, 55.3, 35.4; MS (ESI-TOF) *m/z*: 313 $[M+Na]^+$. HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{17}H_{22}O_4Na$: 313.1416; found: 313.1419.

3-((2*R*,5*R*)-5-(((4-Methoxybenzyl)oxy)methyl)-3-methylenetetrahydrofuran-2-yl)propanal 22: To solution of alcohol **21** (1.74 g, 6 mmol) in THF (12 mL) contained in a pressure tube bis(allyl)-ruthenium(IV) dimer (13 mg, 0.3 mol%), CS_2CO_3 (12 mg, 0.6 mol%)

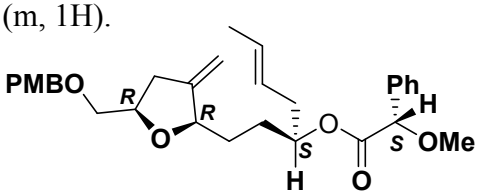
were introduced and reaction mixture was stirred at 80 ^{o}C for 12 h under nitrogen atmosphere. The resulting solution was quenched with satd NaCl (10 mL). The layers were separated and the aq layer was extracted with dichloromethane (3x20 mL). The combined organic exactrats were washed with water (30 mL), brine (30 mL), dried over Na_2SO_4, concentrated and purified by column chromatography over silica gel using 7% EtOAc/Hexane (v/v) as the eluent to furnish compound **22** (1.51 g, 5.22 mmol) in 87% yield as a yellow oil. TLC: R_f 0.3 (10% EtOAc/Hexane); $[\alpha]^{20}_{D}$ +72.2 (*c* 0.55, $CHCl_3$); IR (Neat) 2930, 2856, 1724, 1610, 1513, 1251, 1174, 1094, 1030, 836, 776 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.77 (t, *J* = 1.7 Hz, 1H), 7.27 (d, *J* = 8.7 Hz, 2H), 6.88 (d, *J* = 8.7 Hz, 2H), 5.03 – 4.99 (m, 1H), 4.87 – 4.84 (m, 1H), 4.53 (d, *J* = 11.8 Hz, 1H), 4.48 (d, *J* = 11.8 Hz, 1H), 4.41 – 4.36 (m, 1H), 4.11 – 4.05 (m, 1H), 3.81 (s, 3H), 3.51 – 3.47 (m, 2H), 2.63 – 2.47 (m, 3H), 2.33 – 2.28 (m, 1H), 2.18 – 2.10 (m, 1H), 1.86 – 1.78(m, 1H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 202.6, 159.1, 149.9, 130.1, 129.3, 113.6, 105.2, 79.8, 77.3, 73.0, 71.8, 55.2, 39.4, 36.0, 27.1; MS (ESI-TOF) *m/z*: 313 $[M+Na]^+$. HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{17}H_{22}O_4Na$: 313.1416; found: 313.1422.

(*S*,*E*)-1-((2*R*,5*R*)-5-(((4-Methoxybenzyl)oxy)methyl)-3-methylenetetrahydrofuran-2-yl)hept-5-en-3-ol 23: Tin(II) triflate (25 mg, 0.06 mmol) was added in one portion to a solution of homoallyl alcohol **10** (1.62 g, 10 mmol) and aldehyde **22** (1.45 g, 5 mmol) in $CHCl_3$ (50 mL; passed through a pad of basic Al_2O_3 before use) at rt and the mixture was stirred for 1 h. Subsequently, the mixture was diluted with CH_2Cl_2 (50 mL), washed with a satd $NaHCO_3$ solution (2x50 mL), water (50 mL) and brine (50 mL). The organic layer was dried over sodium sulfate and the solvents were removed in vacuum. The crude compound was purified by column chromatography using 10-20% EtOAc/Hexanes (v/v) as the eluent to afford the alcohol **5** (1.21 g, 3.5 mmol) in 70% yield as a liquid. TLC: R_f 0.3 (10% EtOAc/Hexane); $[\alpha]^{20}_{D}$ +58.4 (*c* 0.5, $CHCl_3$); IR (Neat) 3447, 2922, 2858, 1611, 1512, 1247,

1175, 1035, 970, 821 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.27 (d, *J* = 8.6 Hz, 2H), 6.87 (d, *J* = 8.7 Hz, 2H), 5.59 – 5.50 (m, 1H), 5.49 – 5.40 (m, 1H), 5.0 – 4.95 (m, 1H), 4.86 – 4.82 (m, 1H), 4.54 (d, *J* = 11.8 Hz, 1H), 4.49 (d, *J* = 11.8 Hz, 1H), 4.36 – 4.29 (m, 1H), 4.09 (ddd, *J* = 11.5, 10.1, 5.7 Hz, 1H), 3.80 (s, 3H), 3.67 – 3.59 (m, 1H), 3.52 – 3.49 (m, 2H), 2.6(dd, *J* = 15.7, 6.7 Hz, 1H), 2.41 – 2.31 (m, 1H), 2.27 (bs, 1H), 2.24 – 2.15 (m, 1H), 2.14 – 2.06 (m, 1H), 1.93 – 1.83 (m, 1H), 1.68 (dd, *J* = 6.2, 1.1 Hz, 3H), 1.66 – 1.58 (m, 2H), 1.57 – 1.48 (m, 1H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 159.2, 150.7, 130.2, 129.3, 128.4, 127.4, 113.7, 104.8, 81.3, 77.1, 73.0, 71.9, 70.9, 55.2, 40.7, 36.0, 32.7, 31.3, 18.1; MS (ESI-TOF) *m/z*: 369 $[M+Na]^+$. HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{21}H_{30}O_4Na$: 369.2042; found: 369.2039.



(*R*)-(*S*,*E*)-1-((2*R*,5*R*)-5-(((4-Methoxybenzyl)oxy)methyl)-3-methylenetetrahydrofuran-2-yl)hex-4-en-3-yl 2-methoxy-2-phenylacetate (III): Following the general procedure, alcohol **23** (11 mg, 30 μmol) on reaction with (*R*)-methoxyphenylacetic acid afforded ester **III** (13 mg, 26 μmol) in 89% yield as a liquid. TLC: R_f 0.4 (10% EtOAc/hexanes); ^1H NMR (300 MHz, $CDCl_3$) δ 7.48 – 7.40 (m, 2H), 7.37 – 7.28 (m, 3H), 7.25 (d, *J* = 8.7 Hz, 2H), 6.87 (d, *J* = 8.7 Hz, 2H), 5.51 – 5.38 (m, 1H), 5.37 – 5.24 (m, 1H), 4.97 – 4.85 (m, 1H), 4.85 – 4.80 (m, 1H), 4.72 (s, 1H), 4.52 (d, *J* = 11.8 Hz, 1H), 4.48 – 4.42 (m, 2H), 4.10 – 4.01 (m, 1H), 4.03 – 3.94 (m, 1H), 3.80 (s, 3H), 3.48 – 3.42 (m, 2H), 3.41 (s, 3H), 2.51 (dd, *J* = 15.7, 5.8 Hz, 1H), 2.33 – 2.13 (m, 3H), 1.76 – 1.65 (m, 1H), 1.59 (dd, *J* = 6.1, 1.0 Hz, 3H), 1.56 – 1.30 (m, 2H), 1.23 – 1.07 (m, 1H).



(S)-(S,E)-1-((2R,5R)-5-(((4-methoxybenzyl)oxy)methyl)-3-methylenetetrahydrofuran-2-yl)hex-4-en-3-yl 2-methoxy-2-phenylacetate (IV): Following the general procedure, alcohol **23** (11 mg, , 30 μmol mmol) on reaction with (*S*)-methoxyphenylacetic acid afforded ester **IV** (13.6 mg, , 27 μmol) in 92% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43 (dd, *J* = 7.8, 1.5 Hz, 2H), 7.37 – 730 (m, 3H), 7.26 (d, *J* = 8.7 Hz, 2H), 6.88 (d, *J* = 8.7 Hz, 2H), 5.20 (dq, *J* = 15.6, 6.3 Hz, 1H), 5.07 – 4.97 (m, 1H), 4.97 – 4.91 (m, 2H), 4.75 – 4.72 (m, 1H), 4.72 (s, 1H), 4.55 (d, *J* = 11.8 Hz, 1H), 4.49 (d, *J* = 11.8 Hz, 1H), 4.31 – 4.24 (m, 1H), 4.1 – 4.02 (m, 1H), 3.80 (s, 3H), 3.53 – 3.45 (m, 2H), 3.40 (s, 3H), 2.56 (dd, *J* = 15.6, 6.0 Hz, 1H), 2.35 – 2.25 (m, 1H), 2.09 (t, *J* = 6.8 Hz, 2H), 1.72 – 1.58 (m, 4H),1.43 (dd, *J* = 6.4, 1.2 Hz, 3H). **Note**: The configuration of alcohol **23** was unambiguously established as a '*S*' by comparison of the ^{1}H NMR spectra of (*R*) & (*S*)-mandelate esters. Thus the terminal olefinic protons appeared upfield in the *R*-mandelate compared to the *S*-mandelate while the $CH_2CHCHCH_3$ appeared downfield in the *R*-mandelate ester compared to the *S*-diastereomer.

(2*R*,5*R*)-5-(((4-Methoxybenzyl)oxy)methyl)-2-((*S*,*E*)-3-(methoxymethoxy)hept-5-en-1-yl)-3-methylenetetrahydrofuran 24: To a solution of the alcohol **23** (1 g, 2.9 mmol) and *i*Pr_2NEt (1 mL, 5.8 mmol) in dichloromethane (6 mL) cooled to 0 °C, MOM-Cl (0.33 mL, 4.35 mmol) was added at 0 °C and the resulting reaction mixture was stirred at rt for 2 h. The reaction was quenched with satd aq NH_4Cl (10 mL) and the mixture was extracted with CH_2Cl_2 (3×30 mL). The combined organic layers were washed with brine (30 mL), dried over Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by flash chromatography on silica gel using 5-10% EtOAc/Hexane (v/v) as the eluent to afford the MOM ether **24** (984 mg, 2.52 mmol) in 96% yield as a colourless liquid. TLC: R_f 0.3 (10% EtOAc/Hexane); $[\alpha]^{20}_D$ +57.1 (*c* 0.5, $CHCl_3$); IR (Neat) 2928, 1612, 1513, 1248, 1147,1095,1038, 969, 821 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.27 (d, *J* = 8.7 Hz, 2H), 6.87 (d, *J* = 8.7 Hz, 2H), 5.54 – 5.38 (m, 2H), 4.97 – 4.94 (m, 1H), 4.84 – 4.81 (m, 1H), 4.66 (d, *J*

= 6.9 Hz, 1H), 4.63 (d, *J* = 6.9 Hz, 1H), 4.54 (d, *J* = 11.8 Hz, 1H), 4.49 (d, *J* = 11.8 Hz, 1H), 4.33 – 4.26 (m, 1H), 4.12 – 4.03 (m, 1H), 3.80 (s, 3H), 3.63 – 3.54 (m, 1H), 3.52 (dd, *J* = 10.2, 5.7 Hz, 1H), 3.49 (dd, *J* = 10.2, 4.5 Hz, 1H), 3.37 (s, 3H), 2.58 (dd, *J* = 15.7, 6.0, Hz, 1H), 2.38 – 2.28 (m, 1H), 2.22 (t, *J* = 5.6 Hz, 2H), 1.88 – 1.78 (m, 1H), 1.74 – 1.67 (m, 1H), 1.65 (dd, *J* = 5.8, 0.9 Hz, 3H), 1.61 – 1.45 (m, 2H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 159.1, 151.0, 130.3, 129.3, 127.6, 127.0, 113.7, 104.5, 95.3, 81.2, 77.2, 77.1, 73.0, 72.1, 55.5, 55.2, 37.6, 36.2, 31.0, 29.8, 18.0; MS (ESI-TOF) *m/z*: 413 $[M+Na]^+$. HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{23}H_{34}O_5Na$: 413.2304; found: 413.2303.

((2*R*,5*R*)-5-((*S*,*E*)-3-(Methoxymethoxy)hept-5-en-1-yl)-4-methylenetetrahydrofuran-2-yl)methanol 25: To a solution of PMB ether **24** (0.94 g, 2.4 mmol) in anhydrous dichloromethane (19.8 mL) and pH 7 buffer (2.2 mL) cooled to 0 °C was added DDQ (0.75 g, 3.3 mmol). The reaction mixture was stirred at the same temperature for 2 h and then diluted with water (20 mL). The aq phase was extracted with CH_2Cl_2 (3x50 mL). The combined organic layers were washed with water (50 mL), brine (50 mL), dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. Flash column chromatography using 15% EtOAc/Hexane (v/v) as the eluent afforded alcohol **25** (518 mg, 1.92 mmol) in 80% yield as a colorless oil. TLC: R_f 0.3 (15% EtOAc/Hexane); $[\alpha]^{20}_D$ +51.3 (*c* 0.5, $CHCl_3$); IR (Neat) 3447, 2932, 2857, 1621, 1462, 1388, 1254, 1051, 834, 772 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.55 – 5.38 (m, 2H), 5.0 – 4.95 (m, 1H), 4.85 – 4.81 (m, 1H), 4.68 (d, *J* = 6.9 Hz, 1H), 4.64 (d, *J* = 6.9 Hz, 1H), 4.34 – 4.29 (m, 1H), 4.06 – 3.98 (m, 1H), 3.80 (dd, *J* = 11.8, 3.0 Hz, 1H), 3.66 – 3.59 (m, 1H), 3.54 (dd, *J* = 11.8, 5.1 Hz, 1H), 3.38 (s, 3H), 2.57 – 2.43 (m, 2H), 2.22 (t, *J*= 6.2 Hz, 2H), 1.89 – 1.78 (m, 1H), 1.74 – 1.68 (m, 1H), 1.67 (dd, *J* = 5.9, 1.1 Hz, 3H), 1.65 – 1.49 (m, 2H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 151.1, 127.7, 126.9, 104.8, 95.3, 81.3, 78.2, 77.1, 64.2, 55.5, 37.7, 34.4, 30.9, 30.0, 18.0; MS (ESI-TOF)

m/z: 293 $[M+Na]^+$. HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{15}H_{26}O_4Na$: 293.1729; found: 293.1735.

(2*R*,5*R*)-2-((*S*,*E*)-3-(Methoxymethoxy)hept-5-en-1-yl)-3-methylene-5-((phenylthio)methyl)tetrahydrofuran 7: Following the procedure detailed for the preparation of sulfide **16** from alcohol **15**, alcohol **25** (351 mg, 1.3 mmol) was treated with diphenyl disulfide (312 mg, 1.4 mmol) followed by tri-*n*-butylphosphine (0.64 mL, 2.6 mmol) to afford sulfide **7** (409 mg, 1.13 mmol) in 87% yield as a colourless oil. TLC: R_f 0.3 (10% EtOAc/Hexane); $[\alpha]^{20}_D$ +68.2 (*c* 0.5, $CHCl_3$); IR (Neat) 2924, 2858, 1648, 1451, 1259, 1088, 1031, 800, 741 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.40 – 7.35 (m, 2H), 7.31 – 7.25 (m, 2H), 7.21 – 7.13 (m, 1H), 5.55 – 5.38 (m, 2H), 5.0 – 4.94 (m, 1H), 4.85 – 4.80 (m, 1H), 4.67 (d, *J* = 6.9 Hz, 1H), 4.63 (d, *J* = 6.9 Hz, 1H), 4.32 – 4.26 (m, 1H), 4.11 – 4.03 (m, 1H), 3.61 – 3.53 (m, 1H), 3.37 (s, 3H), 3.23 (dd, *J* = 13.3, 5.1 Hz, 1H), 3.00 (dd, *J* = 13.3, 7.1 Hz, 1H), 2.71 (dd, *J* = 15.5, 6.5 Hz, 1H) 2.42 – 2.32 (m, 1H), 2.22 (t, *J* = 5.7 Hz, 2H), 1.86 – 1.77 (m, 1H), 1.66 (dd, *J* = 5.8, 0.9 Hz, 3H), 1.64 – 1.56 (m, 1H), 1.54 – 1.44 (m, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 150.8, 136.3, 129.2, 128.8, 127.6, 126.9, 126.0, 104.8, 95.3, 81.3, 77.1, 76.8, 55.5, 38.7, 38.5, 37.6, 31.2, 29.8, 18.0; MS (ESI-TOF) *m/z*: 385 $[M+Na]^+$. HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{21}H_{30}O_3NaS$: 385.1813; found: 385.1811.

(2*R*,5*R*)-5-(5-((4-Methoxybenzyl)oxy)-1-(phenylthio)pent-2-yn-1-yl)-2-((*S*,*E*)-3-(methoxymethoxy)hept-5-en-1-yl)-3-methylenetetrahydrofuran 26: To a solution of alkyne **8** (456 mg, 2.4 mmol) in anhydrous THF (0.8 mL) cooled at 0 °C was added *i*PrMgCl·LiCl (1.5 M in THF, 1.6 mL, 2.4 mmol) and the mixture stirred for 30 min at the same temperature. To the so generated Grignard reagent was added a solution of $ZnBr_2$ (1.5 M in THF, 2.4 mL, 3.6 mmol) at 0 °C and the mixture stirred for 30 min. Separately, in another rb flask, the chloro sulfide was prepared by adding a solution of sulfide **7** (290 mg,

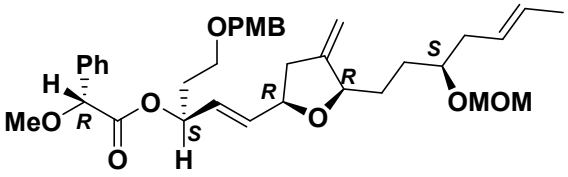
0.8 mmol) in anhydrous benzene (8 mL) to NCS (65 mg, 0.49 mmol) in anhydrous benzene (8 mL) and stirring for 15 min. To the organozinc reagent maintained at 0 °C was added a solution of chloro sulfide in benzene. The reaction mixture was stirred gradually allowing it to attain rt, and stirred further for a period of 2 h when TLC examination indicated complete consumption of the chloro sulfide. The reaction mixture was cooled to 0 °C and quenched by the addition of satd aq NH_4Cl solution (20 mL). It was allowed to warm to rt and diluted with EtOAc (20 mL). The layers were separated and the aq layer was extracted with EtOAc (3x20 mL). The combined organic layers were washed with H_2O (40 mL), brine (40 mL) and dried over anhydrous Na_2SO_4. The solvent was evaporated under reduced pressure to afford a crude compound that was purified by column chromatography using 5% EtOAc/Hexane (v/v) as the eluent to give the pure product **26** (374 mg, 0.68 mmol) in 85% yield as a colourless liquid. TLC: R_f 0.3 (10% EtOAc/Hexane); $[\alpha]^{20}_D$ +19.8 (*c* 0.5, $CHCl_3$); IR (Neat) 2897, 2114, 1648,1614, 1512, 1247, 1030, 925, 860, 741, 503 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.54 – 7.48 (m, 2H), 7.30 – 7.22 (m, 5H), 6.88 (d, *J* = 6.7 Hz, 2H), 5.53 – 5.37 (m, 2H), 5.0 – 4.95 (m, 1H), 4.85 – 4.80 (m, 1H), 4.65 (d, *J* = 6.7 Hz, 1H) 4.63 (d, *J* = 6.7 Hz, 1H), 4.43 (s, 2H), 4.37 – 4.29 (m, 1H), 4.06 – 3.94 (m, 2H), 3.80 (s, 3H), 3.63 – 3.53 (m, 1H), 3.51 – 3.44 (m, 2H), 3.35 (s, 3H), 2.74 – 2.64 (m, 2H), 2.51 – 2.43 (m, 2H), 2.25 – 2.16 (m, 2H), 1.83 – 1.77 (m, 1H), 1.75 – 1.66 (m, 1H), 1.64 (d, *J* = 5.7 Hz, 3H), 1.63 – 1.51 (m, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 159.2, 150.5, 133.8, 130.2, 129.3, 128.7, 128.6, 127.6, 127.0, 113.8, 104.9, 95.3, 83.2, 81.7, 81.4, 79.0, 77.2, 72.6, 68.1, 55.5, 55.3, 43.7, 37.6, 36.6, 31.2, 29.6, 20.2, 18.1; MS (ESI-TOF) *m/z*: 573 $[M+Na]^+$. HRMS (ESI-TOF) *m/z*: $[M+NH_4]^+$ calcd for $C_{33}H_{46}NO_5S$: 568.3097; found: 568.3102.

(*E*)-5-((4-Methoxybenzyl)oxy)-1-((2*R*,5*R*)-5-((*S*,*E*)-3-(methoxymethoxy)hept-5-en-1-yl)-4-methylenetetrahydrofuran-2-yl)pent-1-en-3-one 27: To a solution of sulfide **26** (275 mg, 0.5 mmol) in $CHCl_3$ (1 mL) cooled at -40 °C was added *m*CPBA (70% 123 mg, 0.5 mmol)

and the reaction mixture was stirred at the same temperature for 20 min. Toluene (2 mL) and 2-mercapto-1-methyl-imidazole (86 mg, 0.75 mmol) were added. The reaction mixture was stirred at 60 °C for 2 h and then quenched by the addition of satd aq $NaHCO_3$ (5 mL). The mixture was diluted with CH_2Cl_2 (10 mL) and the layers were separated. The combined organic layers were washed successively with water (20 mL), brine (30 mL) and dried over Na_2SO_4. The solvent was evaporated under reduced pressure to furnish the crude compound which was purified by column chromatography using 5-10% EtOAc/Hexanes (v/v) as the eluent to afford the product **27** (183 mg, 0.4 mmol) in 80% yield as a liquid. TLC: R_f 0.3 (15% EtOAc/Hexane); $[\alpha]^{20}_D$ +33.2 (*c* 0.5, $CHCl_3$); IR (Neat) 2926, 2854, 1675, 1614, 1512, 1451, 1249, 1096, 1035, 813, 749 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.24 (d, *J* = 8.7 Hz, 2H), 6.87 (d, *J* = 8.7 Hz, 2H), 6.82 (dd, *J* = 15.9, 5.3 Hz, 1H), 6.33 (dd, *J* = 15.9, 1.4 Hz, 1H), 5.57 – 5.39 (m, 2H), 5.02 – 4.98 (m, 1H), 4.88 – 4.85 (m, 1H), 4.68 (d, *J* = 6.9 Hz, 1H), 4.64 (d, *J* = 6.9 Hz, 1H), 4.49 – 4.45 (m, 1H), 4.44 (s, 2H), 4.38 – 4.30 (m, 1H), 3.80 (s, 3H), 3.76 (t, *J* = 6.5 Hz, 2H), 3.64 – 3.55 (m, 1H), 3.38 (s, 3H), 2.87 (t, *J* = 6.4 Hz, 2H), 2.75 (dd, *J* = 15.5, 6.2 Hz, 1H), 2.41 – 2.30 (m, 1H), 2.23 (t, *J* = 6.0 Hz, 2H), 1.90 – 1.80 (m, 1H), 1.76 – 1.68 (m, 1H), 1.66 (dd, *J* = 5.9, 1.0 Hz, 3H), 1.62 – 1.48 (m, 2H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 198.4, 159.2, 150.2, 145.2, 130.3, 129.3, 129.1, 127.7, 126.8, 113.7, 105.1, 95.3, 81.4, 77.0, 76.8, 72.9, 65.0, 55.5, 55.2, 40.5, 39.3, 37.6, 31.1, 29.8, 18.0; MS (ESI-TOF) *m/z*: 481 $[M+Na]^+$. HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{27}H_{38}O_6Na$: 481.2566; found: 481.2570.

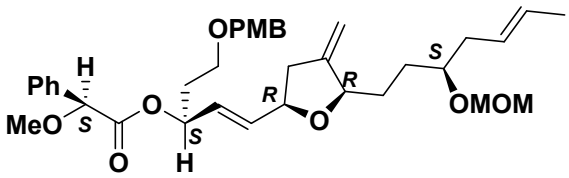
(*S*,*E*)-5-((4-Methoxybenzyl)oxy)-1-((2*R*,5*R*)-5-((*S*,*E*)-3-(methoxymethoxy)hept-5-en-1-yl)-4-methylenetetrahydrofuran-2-yl)pent-1-en-3-ol 28: A solution of (*R*)-(-)-2-methyl-CBS-oxazaborolidine (1 M solution in toluene, 60 µL, 0.06 mmol) in THF (0.4 mL) was treated with BH_3·DMS (57 µL, 0.6 mmol) at -5 ºC. After 1 h the reaction mixture was cooled to -78 ºC. A solution of enone **27** (138 mg, 0.3 mmol) in THF (0.8 mL) was then added

slowly and stirred for 2 h at the same temperature. The reaction was quenched with satd aq NH_4Cl solution (5 mL). The aq layer was extracted with EtOAc (3x15 mL), the combined organic layers were washed with water (20 mL), brine (20 mL), dried over Na_2SO_4 and concentrated. Purification of the residue by column chromatography using 10-20% EtOAc/Hexane (v/v) as the eluent furnished pure alcohol **28** (110 mg, 0.24 mmol) in 80% yield as a colourless oil. TLC: R_f 0.2 (10% EtOAc/hexanes); $[\alpha]^{20}_D$ +35.6 (*c* 0.5, $CHCl_3$); IR (Neat) 3421, 2926, 2854, 1675, 1614, 1512, 1451, 1249, 1096, 1035, 922, 813, 749, 502 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.25 (d, *J* = 8.6 Hz, 2H), 6.88 (d, *J* = 8.6 Hz, 2H), 5.82 – 5.71 (m, 2H), 5.54 – 5.38 (m, 2H), 5.01 – 4.93 (m, 1H), 4.86 – 4.80 (m, 1H), 4.67 (d, *J* = 6.9 Hz, 1H), 4.63 (d, *J* = 6.9 Hz, 1H), 4.44 (s, 2H), 4.35– 4.32 (m, 1H), 4.30 – 4.24 (m, 2H), 3.80 (s, 3H), 3.71 – 3.64 (m, 1H), 3.63 – 3.54 (m, 2H), 3.37 (s, 3H), 2.65 (dd, *J* = 15.5, 5.8 Hz, 1H), 2.38 – 2.27 (m, 1H), 2.22 (t, *J* = 5.8 Hz, 2H), 1.91 – 1.76 (m, 3H), 1.74 – 1.67 (m, 1H), 1.65 (dd, *J* = 5.9, 1.0 Hz, 3H), 1.63 – 1.49 (m, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 159.3, 151.4, 134.8, 130.3, 129.9, 129.3, 127.7, 126.9, 113.8, 104.4, 95.3, 81.0, 78.4, 77.2, 72.9, 71.2, 68.1, 55.5, 55.2, 40.0, 37.6, 36.3, 31.2, 29.8, 18.0; MS (ESI-TOF) *m/z*: 483 $[M+Na]^+$. HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{27}H_{40}O_6Na$: 483.2723; found: 483.2727.



(*R*)-(*S*,*E*)-5-((4-Methoxybenzyl)oxy)-1-((2*R*,5*R*)-5-((*S*,*E*)-3-(methoxymethoxy)hept-5-en-1-yl)-4-methylenetetrahydrofuran-2-yl)pent-1-en-3-yl 2-methoxy-2-phenylacetate (V): Following the general procedure, alcohol **28** (5 mg, 11 μmol) on reaction with (*R*)-methoxyphenylacetic acid (3 mg, 16 μmol) afforded ester **V** (6 mg, 10 μmol) in 91% yield as a liquid. TLC: R_f 0.3 (10% EtOAc/hexanes); ^1H NMR (400 MHz, $CDCl_3$) δ 7.49 – 7.40 (m, 2H), 7.38 – 7.31 (m, 3H), 7.14 (d, *J* = 8.6 Hz, 2H), 6.85 (d, *J* = 8.7 Hz, 2H), 5.76 (dd, *J* =

15.6, 5.8 Hz, 1H), 5.69 (dd, *J* = 15.6, 6.1 Hz, 1H), 5.61 – 5.38 (m, 3H), 4.98 – 4.94 (m, 1H), 4.85 – 4.80 (m, 1H), 4.73 (s, 1H), 4.67 (d, *J* = 6.9 Hz, 1H), 4.63 (d, *J* = 6.9 Hz, 1H), 4.34 – 4.19 (m, 2H), 4.09 (s, 2H), 3.79 (s, 3H), 3.62 – 3.55 (m, 1H), 3.38 (s, 3H), 3.37 (s, 3H), 3.20 – 3.12 (m, 1H), 3.04 – 2.95 (m, 1H), 2.61 (dd, *J* = 15.7, 5.7 Hz, 1H), 2.37 – 2.25 (m, 1H), 2.22 (t, *J* = 5.6 Hz, 2H), 1.92 – 1.68 (m, 4H), 1.65 (dd, *J* = 5.9, 1.1 Hz, 3H) 1.57 – 1.47 (m, 2H).



(*S*)-(*S*,*E*)-5-((4-methoxybenzyl)oxy)-1-((2*R*,5*R*)-5-((*S*,*E*)-3-(methoxymethoxy)hept-5-en-1-yl)-4-methylenetetrahydrofuran-2-yl)pent-1-en-3-yl 2-methoxy-2-phenylacetate (VI): Following the general procedure, alcohol **28** (5 mg, 11 μmol) on reaction with (*S*)-methoxyphenylacetic acid (3 mg, 0.016 mmol) afforded ester **VI** (5.9 mg, 9.6 μmol) in 88% yield as a liquid. TLC: R_f 0.35 (10% EtOAc/hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49 – 7.40 (m, 2H), 7.38 – 7.31 (m, 3H), 7.21 (d, *J* = 8.6 Hz, 2H), 6.86 (d, *J* = 8.7 Hz, 2H), 5.59 – 5.39 (m, 5H), 4.95 – 4.90 (m, 1H), 4.83 – 4.77 (m, 1H), 4.73 (s, 1H), 4.67 (d, *J* = 6.9 Hz, 1H), 4.63 (d, *J* = 6.9 Hz, 1H), 4.32 (s, 2H), 4.27 – 4.19 (m, 1H), 4.15 – 4.07 (m, 1H), 3.79 (s, 3H), 3.62 – 3.55 (m, 1H), 3.45 – 3.38 (m, 5H), 3.37 (s, 3H), 2.48 (dd, *J* = 15.7, 5.7 Hz, 1H), 2.38 – 2.28 (m, 1H), 2.21 (t, *J* = 5.6 Hz, 2H), 1.96 – 1.86 (m, 2H), 1.67 (d, *J* = 5.9 Hz, 3H), 1.58 – 1.44 (m, 4H). **Note**: The configuration of alcohol **28** was unambiguously established as a '*S*' by comparison of the ^{1}H NMR spectra of both (*R*) & (*S*)-mandelate esters. Thus the olefinic protons appeared downfield in the *R*-mandelate compared to the *S*-mandelate while the signals for *CH_2CH_2OPMB* appeared upfield in the *R*-mandelate ester compared to the *S*-diastereomer.

(2*R*,5*R*)-5-((*S*,*E*)-5-((4-Methoxybenzyl)oxy)-3-(methoxymethoxy)pent-1-en-1-yl)-2-((*S*,*E*)-3-(methoxymethoxy)hept-5-en-1-yl)-3-methylenetetrahydrofuran 29: Following

the procedure detailed for the preparation of compound **24** from alcohol **23**, alcohol **28** (92 mg, 0.2 mmol) was treated with *i*Pr$_2$NEt (77 μL, 0.44 mmol) and MOM-Cl (12 μL, 0.15 mmol) to afford MOM ether **29** (93 mg, 0.18 mmol) in 93% yield as a colourless liquid. TLC: R_f 0.2 (5% EtOAc/Hexane); $[\alpha]^{20}_D$ -9.8 (*c* 0.5, $CHCl_3$); IR (Neat) 2897, 1622, 2114, 1512, 1247, 1030, 822 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26 (d, *J* = 8.7 Hz, 2H), 6.88 (d, *J* = 8.7 Hz, 2H), 5.73 (dd, *J* = 15.5, 6.6 Hz, 1H), 5.59 (dd, *J* = 15.5, 7.6 Hz, 1H), 5.54 – 5.35 (m, 2H), 5.00 – 4.93 (m, 1H), 4.85 – 4.80 (m, 1H), 4.68 (d, *J* = 6.9 Hz, 2H), 4.64 (d, *J* = 6.7 Hz, 1H), 4.51 (d, *J* = 6.7 Hz, 1H), 4.42 (s, 2H), 4.34 – 4.25 (m, 2H), 4.24 – 4.18 (m, 1H), 3.80 (s, 3H), 3.63 – 3.54 (m, 2H), 3.54 – 3.48 (m, 1H), 3.37 (s, 3H), 3.34 (s, 3H), 2.65 (dd, *J* = 15.4, 5.7 Hz, 1H), 2.35 – 2.25 (m, 1H), 2.22 (t, *J* = 5.7 Hz, 2H), 1.94 – 1.78 (m, 3H), 1.75 – 1.68 (m, 1H), 1.65 (dd, *J* = 5.9, 0.9 Hz, 3H), 1.60 – 1.47 (m, 2H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 159.1, 151.3, 133.3, 131.8, 130.5, 129.3, 127.6, 126.9, 113.7, 104.4, 95.3, 93.8, 81.0, 78.1, 77.1, 73.2, 72.6, 66.3, 55.5, 55.4, 55.2, 40.1, 37.6, 35.7, 31.2, 29.8, 18.0; MS (ESI-TOF) *m/z*: 527 [M+Na]$^+$. HRMS (ESI-TOF) *m/z*: [M+Na]$^+$ calcd for $C_{29}H_{44}O_7Na$: 527.2985; found: 527.2998.

(*S*,*E*)-3-(Methoxymethoxy)-5-((2*R*,5*R*)-5-((*S*,*E*)-3-(methoxymethoxy)hept-5-en-1-yl)-4-methylenetetrahydrofuran-2-yl)pent-4-en-1-ol 30: Following the procedure detailed for the preparation of compound **25** from PMB ether **24**, compound **29** (70 mg, 0.14 mmol) was treated with DDQ (48 mg, 0.21 mmol) to afford alcohol **30** (43 mg, 0.11 mmol) in 80% yield as a colourless liquid. TLC: R_f 0.2 (20% EtOAc/Hexane); $[\alpha]^{20}_D$ -27.1 (*c* 0.3, $CHCl_3$); IR (Neat) 3281, 2897, 1615, 1512, 1247, 1030, 822 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.75 (dd, *J* = 15.5, 6.6 Hz, 1H), 5.63 (dd, *J* = 15.5, 7.2 Hz, 1H), 5.54 – 5.37 (m, 2H), 4.99 – 4.95 (m, 1H), 4.89 – 4.78 (m, 1H), 4.69 (d, *J* = 6.7 Hz, 1H), 4.67 (d, *J* = 6.9 Hz, 1H), 4.64 (d, *J* = 6.9 Hz, 1H), 4.53 (d, *J* = 6.7 Hz, 1H), 4.33 – 4.25 (m, 3H), 3.83 – 3.77 (m, 1H), 3.74 (dt, *J* = 11.1, 5.5 Hz, 1H), 3.58 (dt, *J* = 11.5, 5.7 Hz, 1H), 3.39 (s, 3H), 3.37 (s, 3H), 2.68 (dd, *J* =

15.4, 5.8 Hz, 1H), 2.36 – 2.28 (m, 1H), 2.22 (t, *J* = 6.1 Hz, 2H), 1.87 – 1.79 (m, 3H), 1.73 – 1.67 (m, 1H), 1.65 (dd, *J* = 5.9, 0.9 Hz, 3H), 1.63 – 1.49 (m, 2H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 151.1, 133.4, 131.4, 127.6, 126.9, 104.6, 95.3, 93.9, 81.1, 78.0, 77.1, 75.0, 59.9, 55.6, 55.5, 40.0, 37.7, 37.6, 31.1, 29.8, 18.0; MS (ESI-TOF) *m/z*: 407 $[M+Na]^+$. HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{21}H_{36}O_6Na$: 407.2410; found: 407.2418.

(*S*,*E*)-3-(Methoxymethoxy)-5-((2*R*,5*R*)-5-((*S*,*E*)-3-(methoxymethoxy)hept-5-en-1-yl)-4-methylenetetrahydrofuran-2-yl)pent-4-enal 3: To a solution of alcohol **30** (35 mg, 90 μmol) in dichloromethane (2 mL) cooled at 0 °C was added Dess−Martin periodinane (60 mg, 0.14 mmol). The mixture was stirred at same temperature for 1.5 h. The reaction was quenched with aq satd $Na_2S_2O_3$ (2 mL). After being stirred for an additional 10 min, the mixture was diluted with CH_2Cl_2 (20 mL) and aq satd NH_4Cl (20 mL). The layers were separated and the aq layer was extracted with CH_2Cl_2 (2x10 mL). The combined organic layers were washed with water (20 mL), brine (20 mL), dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The crude residue was purified by flash column chromatography using 15% EtOAc/Hexane (v/v) as the eluent to afford compound **3** (21 mg, 50 μmol) in 91% yield as a colorless liquid. TLC: R_f 0.5 (15% EtOAc/Hexane); $[\alpha]^{20}_D$ -37.2(*c* 0.5, $CHCl_3$); IR (Neat) 2897, 17.25, 1615, 1512, 1247, 1030, 822, 502 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.77 (t, *J* = 2.6 Hz, 1H), 5.82 (dd, *J* = 15.5, 6.5 Hz, 1H), 5.66 (dd, *J* = 15.5, 7.4 Hz, 1H), 5.54 – 5.36 (m, 2H), 4.99 – 4.93 (m, 1H), 4.85 – 4.80 (m, 1H), 4.68 (d, *J* = 6.8 Hz, 1H), 4.66 (d, *J* = 6.8 Hz, 1H), 4.62 – 4.57 (m, 1H), 4.63 (d, *J* = 6.8 Hz, 1H), 4.45 (d, *J* = 6.8 Hz, 1H), 4.33 – 4.25 (m, 2H), 3.59 – 3.48 (m, 1H), 3.36 (s, 3H), 3.34 (s, 3H), 2.77 – 2.63 (m, 2H), 2.61 – 2.54 (m, 1H), 2.36 – 2.26 (m, 1H), 2.21 (t, *J* = 5.7 Hz, 2H), 1.88 – 1.78 (m, 1H), 1.75 – 1.67 (m, 1H), 1.65 (d, *J* = 5.7 Hz, 3H), 1.62 – 1.47 (m, 2H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 200.3, 150.9, 134.2, 130.0, 127.6, 126.9, 104.7, 95.3, 93.9, 81.1, 77.8,

77.1, 71.2, 55.6, 55.5, 49.0, 40.0, 37.6, 31.1, 29.8, 18.0; MS (ESI-TOF) *m/z*: 405 $[M+Na]^+$. HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{21}H_{34}O_6Na$: 405.2253; found: 405.2250.

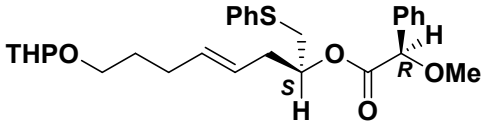
1-Chloro-8-((tetrahydro-2H-pyran-2-yl)oxy)oct-4-yn-2-ol 33: Following the procedure detailed for the preparation of alcohol **13** from alkyne **12** and epoxide **11**, alkyne **32** (4.16 g, 24.75 mmol) was treated with *n*-BuLi (2.5 M in hexane, 10 mL, 25 mmol), $BF_3.OEt_2$ (3 mL, 24.75 mmol) was added followed by (*S*)-epichlorohydrin **31** (1.3 mL, 16.5 mmol) to afford the alcohol **33** (3.81 g, 14.68 mmol) in 89% yield as a colourless oil. TLC: R_f 0.3 (10% EtOAc/Hexane); $[\alpha]^{20}_D$ +3.8 (*c* 0.8, $CHCl_3$); IR (Neat) 3421, 2897, 2114, 1512, 1247, 1030, 822, 743 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 4.60 (t, *J* = 3.1 Hz 1H), 3.94 – 3.88 (m, 1H), 3.87 – 3.82 (m, 1H), 3.81 – 3.75 (m, 1H), 3.69 (dd, *J* = 11.3, 5.9, Hz, 1H), 3.62 (dd, *J* = 11.3, 6.0 Hz, 1H), 3.52 – 3.42 (m, 2H), 2.54 – 2.42 (m, 2H), 2.29 (tt, *J* = 7.2, 2.3 Hz, 2H), 1.85 – 1.63 (m, 4H), 1.62 – 1.50 (m, 4H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 98.8, 82.9, 74.9, 69.9, 65.8, 62.2, 48.2, 30.6, 28.9, 25.4, 24.7, 19.5, 15.6; MS (ESI-TOF) *m/z*: 283 $[M+Na]^+$. HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{13}H_{21}ClO_3Na$: 283.1077; found: 283.1064.

(*2S*)-2-Hydroxy-8-((tetrahydro-2H-pyran-2-yl)oxy)oct-4-yn-1-yl acetate 34: To a stirred solution of chlorohydrin **33** (3.38 g, 13 mmol) in anhydrous DMSO (13 mL) was added KOAc (12.76 g, 130 mmol) and the mixture heated at 120 °C for 6 h when TLC examination revealed complete consumption of starting material. The reaction mixture was cooled to rt, quenched by the addition of water (300 mL) and extracted with $CHCl_3$ (3x50mL). The combined organic layers were washed with brine (100 mL), dried over Na_2SO_4 and evaporated to furnish the crude compound which was purified by column chromatography using 20% EtOAc/Hexane (v/v) as the eluent to afford the pure product **34** (3.36 g, 11.83 mmol) in 91% yield as a viscous oil. TLC: R_f 0.3 (20% EtOAc/Hexane); $[\alpha]^{20}_D$ +2 (*c* 0.9, $CHCl_3$); IR (Neat) 3421, 2897, 2114, 1725,1512, 1247, 1030, 822 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 4.59 (t, *J* = 4.0 Hz, 1H), 4.19 (dd, *J* = 11.4, 4.4 Hz, 1H), 4.11 (dd, *J* = 11.4, 6.5 Hz,

1H), 3.96 – 3.91 (m, 1H), 3.90 – 3.76 (m, 2H), 3.54 – 3.43 (m, 2H), 2.75 (bs, 1H), 2.41 – 2.36 (m, 2H), 2.25 (tt, J = 7.1, 2.3 Hz, 2H), 2.1 (s, 3H), 1.88 – 1.65 (m, 4H), 1.58 – 1.42 (m, 4H); $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ 171.0, 98.7, 82.6, 75.2, 68.2, 67.1, 65.8, 62.2, 30.6, 28.8, 25.3, 24.1, 20.7, 19.4, 15.5; MS (ESI-TOF) *m/z*: 307 $[M+Na]^+$. HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{15}H_{24}O_5Na$: 307.1521; found: 307.1509.

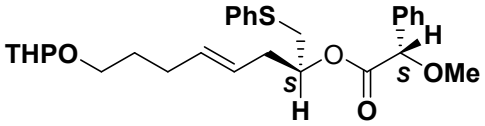
(*2S*)-8-((Tetrahydro-2H-pyran-2-yl)oxy)oct-4-yne-1,2-diol 35: To the suspension of LAH (5 g, 55 mmol) in a mixture of anhydrous THF and toluene (1:1, 17 mL) cooled at 0 °C was added the solution of the homopropargyl alcohol **34** (3.12 g, 11 mmol) in a mixture of THF and toluene (5 mL) dropwise under an atmosphere of nitrogen. The reaction mixture was allowed to attain r.t. and was then heated at 90 °C for 12 h. The reaction mixture was then cooled to 0 °C, diluted with ether (30 mL) and quenched with small pieces of ice. The gel that separated out was filtered, the filter cake washed with EtOAc (2x50 mL) and the filtrate evaporated under reduced pressure. The crude product was purified by flash chromatography on silica gel using 40% EtOAc/Hexane (v/v) as the eluent to afford the homoallyl alcohol **35** (2.55 g, 10.45 mmol) in 95% yield as a colourless oil. TLC: R_f 0.3 (40% EtOAc/Hexane); $[\alpha]^{20}_D$ +11.2 (*c* 0.9, $CHCl_3$); IR (Neat) 3388, 2912, 2864, 1612, 1513, 1247, 1100, 1030, 820 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.57 – 5.49 (m, 1H), 5.48 – 5.39 (m, 1H), 4.57 (t, J = 3.2 Hz, 1H), 3.85 – 3.77 (m, 1H), 3.71– 3.61 (m, 2H), 3.60 – 3.53 (m, 2H), 3.50 (bs, 1H), 3.45 – 3.35 (m, 2H), 3.04 (bs, 1H), 2.16 (t, J = 6.6 Hz, 2H), 2.05 (q, J = 7.1 Hz, 2H), 1.89 – 1.77 (m, 1H), 1.76 – 1.62 (m, 3H), 1.62 – 1.47 (m, 4H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 133.0, 125.8, 98.8, 71.70, 71.66*, 66.8, 66.0, 62.23, 62.21*, 36.5, 30.6, 29.12, 29.06, 25.3, 19.5; MS (ESI-TOF) *m/z*: 267 $[M+Na]^+$. HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{13}H_{24}O_4Na$: 267.1572; found: 267.1566. **Note**: The signals indicated by an asterisk mark compound to diastereomers differing at the anomeric center.

(*2S*)-1-(Phenylthio)-8-((tetrahydro-2H-pyran-2-yl)oxy)oct-4-yn-2-ol 36: Following the procedure detailed for the preparation of sulfide **16** from alcohol **15**, alcohol **35** (2.31 g, 9.5 mmol) was treated with diphenyldisulfide (2.27 g, 10.45 mmol) followed by tri-*n*-butylphosphine (4.68 mL, 19 mmol) to afford sulfide **36** (2.77 g, 8.26 mmol) in 87% yield as a colourless oil. TLC: R_f 0.2 (10% EtOAc/Hexane); $[\alpha]^{20}_D$ +4.5 (*c* 0.25, $CHCl_3$); IR (Neat) 3450, 2907, 2859, 1611, 1511, 1246, 1089, 1031, 967, 819, 741, 691 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.39 – 7.35 (m, 2H), 7.31 – 7.26 (m, 2H), 7.20 (tt, *J* = 7.3, 1.3 Hz, 1H), 5.58 – 5.50 (m, 1H), 5.48 – 5.39 (m, 1H), 4.56 (t, *J* = 4.9 Hz1H), 3.90 – 3.82 (m, 1H), 3.77 – 3.67 (m, 2H), 3.52 – 3.44 (m, 1H), 3.42 – 3.35 (m, 1H), 3.12 (dd, *J* = 13.7, 4.2 Hz, 1H), 2.91 (dd, *J* = 13.7, 8.1 Hz, 1H), 2.50 (d, *J* = 7.9 Hz, 1H), 2.36 – 2.20 (m, 2H), 2.16 – 2.06 (m, 2H), 1.88 – 1.76 (m, 1H), 1.75 – 1.62 (m, 3H), 1.60 – 1.48 (m, 4H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 135.5, 133.9, 129.7, 128.9, 126.4, 125.5, 125.4*, 98.8, 69.10, 69.06*, 66.8, 62.33, 62.31*, 41.0, 39.22, 39.18*, 30.7, 29.29, 29.24*, 25.4, 19.6; MS (ESI-TOF) *m/z*: 359 $[M+Na]^+$. HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{19}H_{28}O_3NaS$: 359.1657; found: 359.1647. **Note**: The signals indicated by an asterisk mark compound to diastereomers differing at the anomeric center.



(2*R*)-(2*S*,*E*)-1-(Phenylthio)-8-((tetrahydro-2H-pyran-2-yl)oxy)oct-4-en-2-yl 2-methoxy-2-phenylacetate (VII): Following the general procedure, alcohol **36** (10 mg, 30 μmol) was reacted with (*R*)-methoxyphenylacetic acid (6.5 mg, 40 μmol) afforded ester **VII** (12.9 mg, 26 μmol) in 89% yield as a liquid. TLC: R_f 0.2 (5% EtOAc/hexanes); ^1H NMR (400 MHz, $CDCl_3$) δ 7.42 – 7.26 (m, 9H), 7.24 – 7.14 (m, 1H), 5.32 – 5.22 (m, 1H), 5.04 – 4.94 (m, 2H), 4.57 (s, 1H), 4.55 (t, *J* = 3.6 Hz, 1H), 3.89 – 3.81 (m, 1H), 3.70 – 3.62 (m, 1H), 3.53 – 3.45 (m, 1H), 3.37 (s, 3H), 3.34 – 3.27 (m, 1H), 3.10 (dd, *J* = 14.0, 6.7 Hz, 1H), 3.03 (dd, *J* = 14.0,

5.7 Hz, 1H), 2.37 – 2.25 (m, 1H), 2.23 – 2.14 (m, 1H), 1.93 – 1.76 (m, 2H), 1.74 – 1.47 (m, 8H).



(2*S*)-(2*S*,*E*)-1-(Phenylthio)-8-((tetrahydro-2H-pyran-2-yl)oxy)oct-4-en-2-yl 2-methoxy-2-phenylacetate (VIII): Following the general procedure, alcohol **36** (10 mg, 30 μmol) was reacted with (*S*)-methoxyphenylacetic acid (6.5 mg, 40 μmol) afforded ester **VIII** (13.2 mg, 27 μmol) in 91% yield as a liquid. TLC: R_f 0.2 (5% EtOAc/hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.47 – 7.42 (m, 2H), 7.40 – 7.31 (m, 5H), 7.28 – 7.23 (m, 2H), 7.19 – 7.14 (m, 1H), 5.50 – 5.42 (m, 1H), 5.31 – 5.23 (m, 1H), 5.04 – 4.96 (m, 1H), 4.75 (s, 1H), 4.59 – 4.53 (m, 1H), 3.89 – 3.83 (m, 1H), 3.74 – 3.68 (m, 1H), 3.53 – 3.46 (m, 1H), 3.43 (s, 3H), 3.38 – 3.32 (m, 1H), 3.00 (dd, *J* = 13.9, 6.5 Hz, 1H), 2.91 (dd, *J* = 13.9, 6.1 Hz, 1H), 2.48 – 2.40 (m, 1H), 2.38 – 2.30 (m, 1H), 2.06 – 1.97 (m, 2H), 1.88 – 1.64 (m, 2H), 1.62 – 1.49 (m, 6H). **Note**: The configuration of alcohol **36** was unambiguously established as a '*S*' by comparison of the ^{1}H NMR spectra of both (*R*) & (*S*)-mandelate esters. Thus the olefinic protons appeared upfield in the *R*-mandelate compared to the *S*-mandelate while the CH_2SPh appeared downfield in the *R*-mandelate ester compared to the *S*-diastereomer.

(*2S*)-1-(Phenylthio)-8-((tetrahydro-2H-pyran-2-yl)oxy)oct-4-yn-2-ylmethanesulfonate 37: Following the procedure detailed for the preparation of compound **16** from alcohol **17**, alcohol **36** (2.45 g, 7.3 mmol) was treated with triethylamine (2 mL, 14.6 mmol) and methanesulfonyl chloride (0.85 mL, 11 mmol) to afford mesylate **37** (2.81 g, 6.79 mmol) in 97% yield as a pale yellow oil, which was used in the next step without further purification. TLC: R_f 0.2 (10% EtOAc/Hexane); IR (Neat) 2935, 2866, 1612, 1513, 1248, 1174, 1095, 917, 818, 743 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 – 7.36 (m, 2H), 7.33 – 7.29 (m, 2H), 7.25 – 7.19 (m, 1H), 5.64 – 5.54 (m, 1H), 5.45 – 5.32 (m, 1H), 4.76 – 4.70 (m, 1H), 4.56 (t, *J*

= 4.6 Hz, 1H), 3.92 – 3.80 (m, 1H), 3.77 – 3.66 (m, 1H), 3.53 – 3.44 (m, 1H), 3.43 – 3.34 (m, 1H), 3.25 (dd, *J* = 14.3, 6.8 Hz, 1H), 3.16 (dd, *J* = 14.3, 6.5 Hz, 1H), 2.96 (s, 3H), 2.61 – 2.56 (m, 1H), 2.55 – 2.46 (m, 1H), 2.12 (q, *J* = 7.2 Hz, 2H), 1.86 – 1.77 (m, 1H), 1.76 – 1.63 (m, 3H), 1.61 – 1.47 (m, 4H); $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$) δ 135.4, 134.8, 129.5, 129.1, 126.6, 123.0, 98.8, 81.0, 66.7, 62.3, 38.4, 37.2, 37.0, 31.5, 30.7, 29.2, 25.4, 19.6; MS (ESI-TOF) *m/z*: 437 $[M+Na]^+$.

(*2R,3R,5R*)-5-((Phenylthio)methyl)-2-(3-((tetrahydro-2H-pyran-2-yl)oxy)propyl)tetrahydrofuran-3-ol 38: Following the procedure detailed for the preparation of alcohol **18** from mesylate **17**, mesylate **37** (2.9 g, 7 mmol) was treated with K_2CO_3 (2.9 g, 21 mmol), $K_3[Fe(CN)_6]$ (6.9 g, 21 mmol) and hydroquinine 1,4-phthalazinediyl diether [$(DHQD)_2PHAL$, 54 mg, 0.07 mmol], methanesulfonamide (4.98 g, 52.5 mmol) and $K_2OsO_2(OH)_4$ (3 mg, 0.007 mmol) in *t*BuOH/H_2O (60 mL, 1:1) to afford tetrahydrofuran derivative **38** (1.6 g, 4.55 mmol) in 65% yield as a viscous liquid. TLC: R_f 0.2 (10% EtOAc/Hexane);$[\alpha]^{20}_D$ +31.5 (*c* 0.25, $CHCl_3$); IR (Neat) 3436, 2925, 1612, 1512, 1246, 1175, 1076, 1033, 820,744, 503 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.42 – 7.38 (m, 2H), 7.29 – 7.23 (m, 2H), 7.17 (t, *J* = 7.3 Hz, 1H), 4.60 – 4.55 (m, 1H), 4.27 – 4.07 (m, 2H), 3.90 – 3.83 (m, 1H), 3.82 – 3.73 (m, 1H), 3.61 (td, *J* = 6.3, 2.7 Hz, 1H), 3.54 – 3.46 (m, 1H), 3.47 – 3.39 (m, 1H), 3.20 (d, *J* = 5.3 Hz, 2H), 2.70 (bs, 1H), 2.43 – 2.33 (m, 1H), 1.87 – 1.67 (m, 6H), 1.65 – 1.46 (m, 5H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 136.2, 129.39, 129.36*, 128.8, 126.10, 126.08*, 99.1, 98.8*, 83.9, 76.0, 72.12, 72.05*, 67.4, 67.3*, 62.5, 62.3*, 39.93, 39.89*, 39.5, 30.7, 30.6*, 26.2, 26.1*, 25.3, 25.28, 25.06*, 19.7, 19.5*; MS (ESI-TOF) *m/z*: 375 $[M+Na]^+$. HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{19}H_{28}O_4NaS$: 375.1618; found: 375.1606. **Note**: The signals indicated by an asterisk mark compound to diastereomers differing at the anomeric center.

(*2R,5R*)-5-((Phenylthio)methyl)-2-(3-((tetrahydro-2H-pyran-2-yl)oxy)propyl)dihydrofuran-3(2H)-one 39: To a stirred solution of 2-iodoxybenzoic acid (1.76 g, 6.3 mmol) in anhydrous DMSO (8.4 mL) cooled at 0 °C was added a solution of alcohol **38** (1.58 g, 4.2 mmol) in anhydrous CH_2Cl_2 (13 mL) and the reaction mixture stirred for a period of 2 h at rt. After completion of the reaction, the mixture was filtered through a small Celite pad. The filtrate was diluted with CH_2Cl_2 (50 mL), washed with water (100 mL), brine (50 mL) and dried over Na_2SO_4. The solvent was evaporated under reduced pressure to afford the residue which was purified by column chromatography using 5-10% EtOAc/hexane (v/v) as the eluent to give the pure ketone **39** (1.32 g, 3.78 mmol) in 90% yield as a colourless liquid. TLC: R_f 0.3 (10% EtOAc/hexane); $[\alpha]^{20}_D$ +35.4 (*c* 0.5, $CHCl_3$); IR (Neat) 2908, 2862, 1758, 1611, 1512, 1247, 1173, 1089, 1031, 820, 743, 693, 502 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.43 – 7.38 (m, 2H), 7.33 – 7.27 (m, 2H), 7.21 (tt, *J* = 7.3, 1.2, Hz, 1H), 4.56 (t, *J* = 3.5 Hz, 1H), 4.41 – 4.28 (m, 1H), 3.87 – 3.79 (m, 2H), 3.77 – 3.67 (m, 1H), 3.56 – 3.45 (m, 1H), 3.42 – 3.33 (m, 1H), 3.30 (dd, *J* = 13.7, 5.0 Hz, 1H), 3.18 (dd, *J* = 13.7, 6.8 Hz, 1H), 2.60 (dd, *J* = 18.1, 5.7 Hz, 1H), 2.33 (dd, *J* = 18.1, 10.2 Hz, 1H), 1.98 – 1.76 (m, 3H), 1.76 – 1.43 (m, 7H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 214.9, 135.5, 129.9, 129.0, 126.6, 98.7, 81.5, 74.7, 66.9, 66.8*, 62.2, 42.4, 38.8, 30.7, 27.9, 27.8*, 25.5, 25.4, 25.3*, 19.5; MS (ESI-TOF) *m/z*: 373 $[M+Na]^+$. HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{19}H_{26}O_4NaS$: 373.1449; found: 373.1446. **Note**: The signals indicated by an asterisk mark compound to diastereomers differing at the anomeric center.

2-(3-((2*R*,5*R*)-3-Methylene-5-((phenylthio)methyl)tetrahydrofuran-2-yl)propoxy)tetrahydro-2H-pyran 40: Methyltriphenylphosphonium bromide (6.25 g, 17.5 mmol) was suspended in anhydrous THF (20 mL) and a solution of potassium *tert*-butoxide solution (1.76 g, 15.75 mmol) in anhydrous THF (10 mL) was added dropwise at 0 °C. The resultant yellow solution was stirred for 45 min and was added to the solution of ketone **39**

(1.22 g, 3.5 mmol) in anhydrous THF (5 mL) at 0 °C. The reaction mixture was stirred for 30 min and then quenched with H_2O (30 mL). The mixture was extracted with EtOAc (3x50 mL). The combined organic extracts were washed with brine (50 mL), dried over anhydrous Na_2SO_4, filtered and concentrated. The residue was purified by silica gel column chromatography using 3% EtOAc/Hexane (v/v) as the eluent to afford the pure compound **40** (1.1 g, 3.18 mmol) in 91% yield as a colourless oil. TLC: R_f 0.3 (5% EtOAc/Hexane); $[\alpha]^{20}_D$ +43.4 (*c* 0.5, $CHCl_3$); IR (Neat) 2903, 2860, 1611, 1512, 1247, 1175, 1087, 1033, 819, 741, 692 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.41 – 7.34 (m, 2H), 7.30 – 7.25 (m, 2H), 7.21 – 7.13 (tt, *J* = 7.3, 1.2 Hz, 1H), 4.99 – 4.95 (m, 1H), 4.86 – 4.82 (m, 1H), 4.60 – 4.56 (m, 1H), 4.36 – 4.30 (m, 1H), 4.13 – 4.01 (m, 1H), 3.90 – 3.83 (m, 1H), 3.79 – 3.71 (m, 1H), 3.53 – 3.46 (m, 1H), 3.45 – 3.37 (m, 1H), 3.24 (dd, *J* = 13.2, 5.2 Hz, 1H), 3.00 (dd, *J* = 13.2, 7.1 Hz, 1H), 2.72 (dd, *J* = 15.6, 5.8 Hz, 1H), 2.42 – 2.32 (m, 1H), 1.88 – 1.66 (m, 5H), 1.65 – 1.46 (m, 5H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 150.7, 133.8, 133.6*, 129.3, 128.9*, 128.5, 128.4*, 126.0, 105.0, 98.8, 81.03, 80.97*, 76.8, 67.5, 67.4*, 62.31, 62.27*, 38.8, 38.5*, 32.0, 31.9*, 30.7, 29.7, 25.5, 25.4, 19.6; MS (ESI-TOF) *m/z*: 371 $[M+Na]^+$. HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{20}H_{28}O_3NaS$: 371.1657; found: 371.1656. **Note**: The signals indicated by an asterisk mark compound to diastereomers differing at the anomeric center.

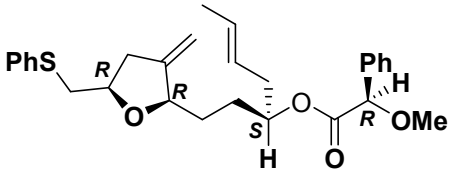
3-((2*R*,5*R*)-3-Methylene-5-((phenylthio)methyl)tetrahydrofuran-2-yl)propan-1-ol 41: To solution of THP ether **40** (870 mg, 2.5 mmol) in methanol (5 mL) was added PTSA (20 mg, 0.11) and the mixture stirred at rt for 12 h. The solvent was evaporated and the residue was dissolved in ethyl acetate (20 mL) and washed with satd aq $NaHCO_3$ (20 mL), water (20 mL), brine (20 mL) and dried over anhydrous Na_2SO_4. After filtration, the solvent was evaporated under reduced pressure and the crude product was purified by flash column chromatography using 10-20% EtOAc/Hexane (v/v) as the eluent to afford the primary alcohol **41** (627 mg, 2.37 mmol) in 95% yield as a colorless oil. TLC: R_f 0.3 (20% EtOAc/Hexane); $[\alpha]^{20}_D$ +50.2

(c 0.5, $CHCl_3$); IR (Neat) 3417, 2924, 2858, 1614, 1512, 1247, 1175, 1094, 1030, 820 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.41 – 7.35 (m, 2H), 7.32 – 7.25 (m, 2H), 7.18 (tt, J = 7.3, 1.2 Hz, 1H), 5.01 – 4.94 (m, 1H), 4.86 – 4.82 (m, 1H), 4.35 – 4.29 (m, 1H), 4.12– 4.04 (m, 1H), 3.71– 3.60 (m, 2H), 3.22 (dd, J = 13.3, 5.5 Hz, 1H), 3.03 (dd, J = 13.3, 6.9 Hz, 1H), 2.73 (dd, J = 15.5, 5.7 Hz, 1H), 2.49 – 2.35 (m, 1H), 1.91 – 1.80 (m, 1H), 1.79 – 1.54 (m, 4H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 150.4, 136.1, 129.5, 128.9, 126.2, 105.2, 81.2, 76.8, 62.9, 38.6, 38.5, 32.1, 29.0; MS (ESI-TOF) *m/z*: 287 $[M+Na]^+$. HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{15}H_{20}O_2NaS$: 287.1082; found: 287.1099.

3-((2*R*,5*R*)-3-Methylene-5-((phenylthio)methyl)tetrahydrofuran-2-yl)propanal 42: Following the procedure detailed for the preparation of ketone **39** from alcohol **38**, alcohol **41** (475 mg, 1.8 mmol) was treated with 2-iodoxybenzoic acid (756 mg, 2.7 mmol) in anhydrous DMSO and dichloromethane to afford aldehyde **42** (405 mg, 1.54 mmol) in 86% yield as a colourless oil. TLC: R_f 0.3 (10% EtOAc/Hexane); $[\alpha]^{20}_D$ +63.1 (c 0.5, $CHCl_3$); IR (Neat) 2930, 2856, 1724, 1610, 1513, 1251, 1174, 1094, 1030, 836, 776 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 9.68 (t, J = 1.5 Hz, 1H), 7.37 – 7.26 (m, 2H), 7.25 – 7.18 (m, 2H), 7.11 (t, J = 7.3 Hz, 1H), 5.01 – 4.94 (m, 1H), 4.87 – 4.83 (m, 1H), 4.33 – 4.27 (m, 1H), 4.05 – 3.96 (m, 1H), 3.13 (dd, J = 13.4, 5.3 Hz, 1H), 2.96 (dd, J = 13.4, 6.6 Hz, 1H), 2.65 (dd, J = 15.7, 5.7 Hz, 1H), 2.52 – 2.37 (m, 2H), 2.36 – 2.20 (m, 1H), 2.12 – 1.99 (m, 1H), 1.79 – 1.69 (m, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 202.4, 149.9, 136.2, 129.3, 128.9, 126.1, 105.6, 79.9, 77.1, 39.5, 38.7, 38.3, 27.4; MS (ESI-TOF) *m/z*: 285 $[M+Na]^+$. HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{15}H_{18}O_2NaS$: 285.0925; found: 285.0935.

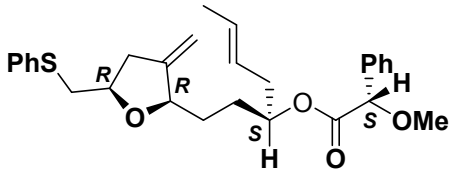
(*S*,*E*)-1-((2*R*,5*R*)-3-Methylene-5-((phenylthio)methyl)tetrahydrofuran-2-yl)hept-5-en-3-ol 44: To a solution of aldehyde **42** (314 mg, 1.2 mmol) and alcohol **43** (630 mg, 3 mmol) in anhydrous dichloromethane (6 mL), PTSA (25 mg, 0.135 mmol) was slowly added. After stirring at rt for 12 h, then the reaction was cooled to 0 °C and quenched by addition of satd

$NaHCO_3$ solution (5 mL). The reaction mixture was extracted with CH_2Cl_2 (3x15 mL). The combined organic layers were washed with H_2O (20 mL), brine (20 mL) and dried over anhydrous Na_2SO_4, filtered and concentrated. Purification of the residue by flash column chromatography using 10-20% EtOAc/Hexanes (v/v) as the eluent to afford the alcohol **44** (297 mg, 0.93 mmol) in 78% yield as a liquid. TLC: R_f 0.3 (15% EtOAc/Hexane); $[\alpha]^{20}_D$ +66.1 (*c* 0.5, $CHCl_3$); IR (Neat) 3447, 2922, 2858, 1611, 1512, 1247, 1175, 1035, 970, 821 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.40 – 7.35 (m, 2H), 7.31 – 7.27 (m, 2H), 7.19 (tt, *J* = 7.3, 1.2 Hz, 1H), 5.59 – 5.50 (m, 1H), 5.48 – 5.40 (m, 1H), 4.99 – 4.95 (m, 1H), 4.86 – 4.82 (m, 1H), 4.32 – 4.28 (m, 1H), 4.12 – 4.04 (m, 1H), 3.64 – 3.58 (m, 1H), 3.23 (dd, *J* = 13.3, 5.3 Hz, 1H), 3.02 (dd, *J* = 13.3, 7.0 Hz, 1H), 2.73 (dd, *J* = 15.7, 5.9 Hz, 1H), 2.43 – 2.35 (m, 1H), 2.23 – 2.17 (m, 1H), 2.09 (t, *J* = 7.2 Hz, 2H), 1.93 – 1.83 (m, 1H), 1.69 (dd, *J* = 6.2, 1.1 Hz, 3H), 1.67 – 1.59 (m, 1H), 1.56 – 1.47 (m, 1H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 150.6, 136.2, 129.4, 128.9, 128.6, 127.2, 126.1, 105.1, 81.4, 76.8, 70.9, 40.7, 38.7, 38.5, 32.6, 31.5, 18.1; MS (ESI-TOF) *m/z*: 341 $[M+Na]^+$. HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{19}H_{26}O_2NaS$: 341.1551; found: 341.1556.



(*R*)-(*S*,*E*)-1-((2*R*,5*R*)-3-Methylene-5-((phenylthio)methyl)tetrahydrofuran-2-yl)hex-4-en-3-yl 2-methoxy-2-phenylacetate (IX): Following the general procedure, alcohol **44** (6 mg, 20 μmol) was reacted with (*R*)-methoxyphenylacetic acid (5 mg, 30 μmol) to furnish ester **IX** (8.7 mg, 18 μmol) in 93% yield as a liquid. TLC: R_f 0.4 (10% EtOAc/hexanes); ^1H NMR (400 MHz, $CDCl_3$) δ 7.47 7.43 (m, 2H), 7.39 – 7.25 (m, 7H), 7.20 – 7.14 (m, 1H), 5.50 – 5.40 (m, 1H), 5.36 – 5.26 (m, 1H), 4.95 – 4.86 (m, 1H), 4.85 – 4.82 (m, 1H), 4.71 (s, 1H), 4.51 – 4.47 (m, 1H), 4.07 – 4.02 (m, 1H), 4.02 – 3.95 (m, 1H), 3.41 (s, 3H), 3.15 (dd, *J* =

13.3, 5.1 Hz, 1H), 2.91 (dd, *J* = 13.3, 7.1 Hz, 1H), 2.63 (dd, *J* = 16.1, 6.3 Hz, 1H), 2.37 – 2.19 (m, 4H), 1.61 (dd, *J* = 6.3, 1.3 Hz, 3H), 155 – 1.45 (m, 3H).



(*S*)-(*S*,*E*)-1-((2*R*,5*R*)-3-Methylene-5-((phenylthio)methyl)tetrahydrofuran-2-yl)hex-4-en-3-yl 2-methoxy-2-phenylacetate (X): Following the general procedure, alcohol **44** (6 mg, 20 μmol) was reacted with (*S*)-methoxyphenylacetic acid (5 mg, 30 μmol) to furnish ester **X** (8.5 mg, 18 μmol) in 91% yield as a liquid. TLC: R_f 0.35 (10% EtOAc/hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44 (dd, *J* = 7.8, 1.7 Hz, 2H), 7.39 – 7.27 (m, 7H), 7.20 – 7.15 (m, 1H), 5.24 – 5.16 (m, 1H), 5.08 – 4.98 (m, 1H), 4.96 – 4.88 (m, 2H), 4.73 (s, 1H), 4.72 – 4.69 (m, 1H), 4.26 – 4.21 (m, 1H), 4.07 – 4.02m, 1H), 3.41 (s, 3H), 3.20 (dd, *J* = 13.3, 5.2 Hz, 1H), 2.98 (dd, *J* = 13.3, 7.0 Hz, 1H), 2.69 (dd, *J* = 15.2, 6.3 Hz, 1H), 2.40 – 2.28 (m, 3H), 2.16 – 1.96 (m, 2H), 1.69 – 1.58 (m, 2H), 1.45 (dd, *J* = 6.3, 1.3 Hz, 3H). **Note**: The configuration of alcohol **44** was unambiguously established as '*S*' by comparison of the ^{1}H NMR spectra of both (*R*) & (*S*)-mandelate esters. Thus the terminal olefinic protons appeared upfield in the *R*-mandelate compared to the *S*-mandelate while the signals for $CH_2CHCHCH_3$ appeared downfield in the *R*-mandelate ester compared to the *S*-diastereomer.

(2*R*,5*R*)-2-((*S*,*E*)-3-(Methoxymethoxy)hept-5-en-1-yl)-3-methylene-5-((phenylthio)methyl)tetrahydrofuran 7: Following the procedure detailed for the preparation of compound **24** from alcohol **23**, alcohol **44** (222 mg, 0.7 mmol) was treated with *i*Pr_2NEt (0.24 mL, 1.4 mmol) and MOM-Cl (75 μL, 1 mmol) to afford MOM ether **7** (242 mg, 0.67 mmol) in 96% yield as a colourless liquid.

***tert*-Butyl(((*S*)-5-((2*R*,5*R*)-5-((*S*,*E*)-3-(methoxymethoxy)hept-5-en-1-yl)-4-methylenetetrahydrofuran-2-yl)-5-(phenylthio)pent-3-yn-1-yl)oxy)diphenylsilane 45:** To a solution of alkyne (415 mg, 1.35 mmol) in anhydrous THF (0.5 mL) cooled at 0 °C was

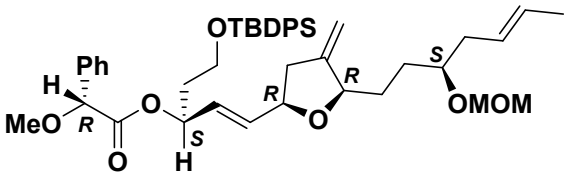
added *i*PrMgCl·LiCl (1.5 M in THF, 0.9 mL, 1.35 mmol) and the mixture stirred for 30 min at the same temperature. To the so generated Grignard reagent was added a solution of $ZnBr_2$ (1.5 M in THF, 1.35 mL, 2 mmol) at 0 °C and the mixture stirred for 30 min. Separately, in another rb flask, the chloro sulfide was prepared by adding a solution of sulfide **7** (163 mg, 0.45 mmol) in anhydrous benzene (5 mL) to NCS (65 mg, 0.49 mmol) in anhydrous benzene (5 mL) and stirring for 15 min. To the organozinc reagent maintained at 0 °C was added a solution of chloro sulfide in benzene. The reaction mixture was stirred gradually allowing it to attain rt, and stirred further for a period of 4 h when TLC examination indicated complete consumption of the chloro sulfide. The reaction mixture was cooled to 0 °C and quenched by the addition of satd aq NH_4Cl solution (20 mL). It was allowed to warm to rt and diluted with EtOAc (20 mL). The layers were separated and the aq layer was extracted with EtOAc (3x20 mL). The combined organic layers were washed with H_2O (40 mL), brine (40 mL) and dried over anhydrous Na_2SO_4. The solvent was evaporated under reduced pressure to afford a crude compound that was purified by column chromatography using 5% EtOAc/Hexane (v/v) as the eluent to give the pure product **45** (254 mg, 0.38 mmol) in 85% yield as a colourless liquid. TLC: R_f 0.3 (5% EtOAc/Hexane); $[\alpha]^{20}_D$ +26.7 (*c* 1, $CHCl_3$); IR (Neat) 2897, 2114, 1648, 1512, 1247, 1030, 925, 860, 741, 503 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.77 – 7.58 (m, 4H), 7.51 – 7.32 (m, 9H), 7.24 – 7.15 (m, 2H), 5.55 – 5.35 (m, 2H), 4.95 – 4.91 (m, 1H), 4.82– 4.78 (m, 1H), 4.65 (d, *J* = 6.8 Hz, 1H), 4.62 (d, *J* = 6.8 Hz, 1H), 4.36 – 4.28 (m, 1H), 4.04 – 3.93 (m, 2H), 3.66 (t, *J* = 7.2 Hz, 2H), 3.58 – 3.52 (m, 1H), 3.35 (s, 3H), 2.74 – 2.61 (m, 2H), 2.48 – 2.38 (m, 2H), 2.19 (t, *J* = 5.6 Hz, 2H), 1.84 – 1.66 (m, 2H), 1.64 (d, *J* = 5.3 Hz, 3H), 1.61 – 1.47 (m, 2H), 1.04 (s, 9H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 150.5, 135.5, 133.8, 133.6, 133.0, 129.7, 128.7, 127.7, 127.6, 127.0, 104.8, 95.3, 83.4, 81.7, 79.1, 77.4, 77.1, 62.4, 55.5, 43.9, 37.6, 36.8, 31.2, 29.7, 26.8, 23.0, 19.2, 18.0; MS 691 (ESI-TOF) *m/z*:

[M+Na]$^+$. HRMS (ESI-TOF) *m/z*: [M+Na]$^+$ calcd for $C_{41}H_{52}O_4NaSSi$: 691.3253; found: 691.3240.

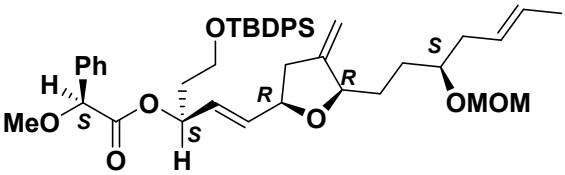
(*E*)-5-((*tert*-Butyldiphenylsilyl)oxy)-1-((2*R*,5*R*)-5-((*S*,*E*)-3-(methoxymethoxy)hept-5-en-1-yl)-4-methylenetetrahydrofuran-2-yl)pent-1-en-3-one 46: Following the procedure detailed for the preparation of compound **27** from sulfide **26**, sulfide **45** (200 mg, 0.3 mmol) was treated with *m*CPBA (70%, 78 mg, 0.29 mmol) followed by 2-mercapto-1-methylimidazole (69 mg, 0.6 mmol) to afford the product **46** (138 mg, 0.24 mmol) in 80% yield as a liquid. TLC: R_f 0.2 (15% EtOAc/Hexanes); $[\alpha]^{20}_D$ +35.2 (*c* 1, $CHCl_3$); IR (Neat) 2926, 2854, 1675, 1614, 1512, 1451, 1249, 1096, 1035, 813, 749, 505 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 – 7.62 (m, 4H), 7.44 – 7.35 (m, 6H), 6.78 (dd, *J* = 15.9, 5.3 Hz, 1H), 6.34 (dd, *J* = 15.9, 1.4 Hz, 1H), 5.55 – 5.39 (m, 2H), 5.03 – 4.99 (d, *J* = 1.5 Hz, 1H), 4.89 – 4.85 (d, *J* = 1.5 Hz, 1H), 4.68 (d, *J* = 6.9 Hz, 1H),4.62 (d, *J* = 6.9 Hz, 1H), 4.48 – 4.42 (m, 1H), 4.37 – 4.31 (m, 1H), 3.98 (t, *J* = 6.4 Hz, 2H), 3.63 – 3.56 (m, 1H), 3.38 (s, 3H), 2.81 (td, *J* = 6.5, 1.6 Hz, 2H), 2.75 (dd, *J* = 15.1, 5.9 Hz, 1H), 2.41 – 2.31 (m, 1H), 2.24 (t, *J* = 5.9 Hz, 2H), 1.90 – 1.82 (m, 1H), 1.78 – 1.70 (m, 1H), 1.67 (dd, *J* = 5.8, 0.9 Hz, 3H), 1.64 – 1.52 (m, 2H), 1.02 (s, 9H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 199.0, 150.2, 145.0, 135.5, 133.5, 129.6, 129.5, 127.71, 127.66, 126.9, 105.1, 95.4, 81.4, 77.1, 76.8, 59.8, 55.5, 43.0, 39.3, 37.6, 31.1, 29.9, 26.8, 19.1, 18.1; MS (ESI-TOF) *m/z*: 599 [M+Na]$^+$. HRMS (ESI-TOF) *m/z*: [M+Na]$^+$ calcd for $C_{35}H_{48}O_5NaSi$: 599.3169; found: 599.3175.

(*S*,*E*)-5-((*tert*-Butyldiphenylsilyl)oxy)-1-((2*R*,5*R*)-5-((*S*,*E*)-3-(methoxymethoxy)hept-5-en-1-yl)-4-methylenetetrahydrofuran-2-yl)pent-1-en-3-ol 47: Following the procedure detailed for the preparation of alcohol **28** from enone **27**, enone **46** (115 mg, 0.2 mmol) on reduction with (*R*)-(−)-2- methyl-CBS-oxazaborolidine (1 M solution in toluene, 40 µL, 0.04 mmol) and BH_3·DMS (37 µL, 0.4 mmol) at 0 to −78 °C afforded alcohol **47** (93 mg, 0.16 mmol) in 80% yield as a colourless oil. TLC: R_f 0.2 (20% EtOAc/Hexanes); $[\alpha]^{20}_D$ +46.9 (*c*

1, $CHCl_3$); IR (Neat) 3421, 2926, 2854, 1675, 1614, 1512, 1451, 1249, 1096, 1035, 922, 813, 749, 502 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.74 – 7.63 (m, 4H), 7.48 – 7.36 (m, 6H), 5.86 – 5.74 (m, 2H), 5.54 – 5.37 (m, 2H), 4.99 – 4.95 (m, 1H), 4.85 – 4.81 (m, 1H), 4.67 (d, *J* = 6.9 Hz, 1H), 4.64 (d, *J* = 6.9 Hz, 1H), 4.48 – 4.43 (m, 1H), 4.33 – 4.25 (m, 2H), 3.93 – 3.79 (m, 2H), 3.63 – 3.53 (m, 1H), 3.37 (s, 3H), 3.24 (d, *J* = 3.3 Hz, 1H), 2.66 (dd, *J* = 15.7, 5.8 Hz, 1H), 2.41 – 2.29 (m, 1H), 2.22 (t, *J* = 5.6 Hz, 2H), 1.87 – 1.75 (m, 3H), 1.74 – 1.68 (m, 1H), 1.65 (dd, *J* = 5.2, 1.6 Hz, 3H), 1.63 – 1.51 (m, 2H), 1.1 (s, 9H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 151.5, 135.5, 134.9, 133.0, 130.2, 129.8, 127.8, 127.6, 127.0, 104.4, 95.3, 81.0, 78.4, 77.2, 71.4, 62.7, 55.5, 40.0, 38.4, 37.6, 31.2, 29.9, 26.8, 19.0, 18.0; MS (ESI-TOF) *m/z*: 601 $[M+Na]^+$. HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{35}H_{50}O_5NaSi$: 601.3325; found: 601.3323.



(*R*)-(*S*,*E*)-5-((*tert*-Butyldiphenylsilyl)oxy)-1-((2*R*,5*R*)-5-((*S*,*E*)-3-(methoxymethoxy)hept-5-en-1-yl)-4-methylenetetrahydrofuran-2-yl)pent-1-en-3-yl 2-methoxy-2-phenylacetate (XI): Following the general procedure, alcohol **47** (5 mg, 10 μmol) was reacted with (*R*)-methoxyphenylacetic acid (3 mg, 0.02 mmol) to furnish ester **XI** (6.8 mg, 9.4 μmol) in 94% yield as a liquid. TLC: R_f 0.4 (10% EtOAc/hexanes); ^1H NMR (500 MHz, $CDCl_3$) δ 7.59 – 7.53 (m, 4H), 7.43 – 7.39 (m, 2H), 7.38 – 7.35 (m, 6H), 7.26 – 7.23 (m, 3H), 5.74 (dd, *J* = 15.5, 5.8 Hz, 1H), 5.69 (dd, *J* = 15.6, 6.1 Hz, 1H), 5.60 – 5.53 (m, 1H), 5.53 – 5.39 (m, 2H), 4.97 – 4.93 (m, 1H), 4.84 – 4.81 (m, 1H), 4.70 (s, 1H), 4.67 (d, *J* = 6.9 Hz, 1H), 4.63 (d, *J* = 6.9 Hz, 1H), 4.32 – 4.24 (m, 1H), 4.24 – 4.18 (m, 1H), 3.61 – 3.55 (m, 1H), 3.46 3.41 (m, 1H), 3.40 – 3.38 (m, 1H), 3.37 (s, 3H), 3.36 (s, 3H), 2.58 (dd, *J* = 15.8, 5.7 Hz, 1H), 2.38 – 2.25 (m, 1H), 2.22 (t, *J* = 6.0, Hz, 2H), 2.08 – 1.97 (m, 1H), 1.87 – 1.67 (m, 3H), 1.65 (dd, *J* = 5.9, 1.0 Hz, 3H), 1.62 – 1.57 (m, 1H), 1.54 – 1.46 (m, 1H), 0.99 (s, 9H).



(*S*)-(*S*,*E*)-5-((*tert*-Butyldiphenylsilyl)oxy)-1-((2*R*,5*R*)-5-((*S*,*E*)-3-(methoxymethoxy)hept-5-en-1-yl)-4-methylenetetrahydrofuran-2-yl)pent-1-en-3-yl 2-methoxy-2-phenylacetate (XII): Following the general procedure, alcohol **47** (5 mg, 10 μmol) was reacted with (*S*)-methoxyphenylacetic acid (3 mg, 0.02 mmol) to furnish ester **XII** (6.9 mg, 9.5 μmol) in 95% yield as a liquid. TLC: R_f 0.35 (10% EtOAc/hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66 – 7.60 (m, 4H), 7.43 – 7.35 (m, 8H), 7.34 – 7.27 (m, 3H), 5.62 – 5.39 (m, 5H), 4.94 – 4.90 (m, 1H), 4.81 – 4.78 (m, 1H), 4.69 – 4.66 (m, 2H), 4.63 (d, *J* = 6.9 Hz, 1H), 4.25 – 4.18 (m, 1H), 4.11 – 4.04 (m, 1H), 3.64 (t, *J* = 6.2 Hz, 2H), 3.60 – 3.54 (m, 1H), 3.37 (s, 3H), 3.36 (s, 3H), 2.44 (dd, *J* = 15.5, 5.7 Hz, 1H), 2.22 (t, *J* = 5.7 Hz, 2H), 2.15 – 2.05 (m, 1H), 1.90 – 1.75 (m, 3H), 1.65 (d, *J* = 5.0 Hz, 3H), 1.57 – 1.40 (m, 3H), 1.03 (s, 9H). **Note**: The configuration of alcohol **47** was unambiguously established as a '*S*' by comparison of the ^{1}H NMR spectra of both (*R*) & (*S*)-mandelate esters. Thus the olefinic protons appeared downfield in the *R*-mandelate compared to the *S*-mandelate while the signals for *$CH_2CH_2OTBDPS$* appeared upfield in the *R*-mandelate ester compared to the *S*-diastereomer.

(S)-5-((*E*)-2-((2*R*,5*R*)-5-((*S*,*E*)-3-(Methoxymethoxy)hept-5-en-1-yl)-4-methylenetetrahydrofuran-2-yl)vinyl)-10,10-dimethyl-9,9-diphenyl-2,4,8-trioxa-9-silaundecane 48: Following the procedure detailed for the preparation of compound **24** from alcohol **23**, alcohol **47** (75 mg, 0.13 mmol) was treated with *i*Pr_2NEt (45 μL, 0.26 mmol) and MOM-Cl (15 μL, 0.2 mmol) to afford MOM ether **48** (74 mg, 0.12 mmol) in 93% yield as a colourless liquid. TLC: R_f 0.2 (5% EtOAc/Hexane); $[\alpha]^{20}_D$ -6.2 (*c* 1, $CHCl_3$); IR (Neat) 2897, 1612, 1512, 1247, 1030, 822, 501 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69 – 7.63 (m, 4H), 7.47 – 7.33 (m, 6H), 5.73 (dd, *J* = 15.6, 6.6 Hz, 1H), 5.59 (dd, *J* = 15.5, 7.6 Hz, 1H), 5.54 – 5.37 (m, 2H), 4.98 – 4.94 (m, 1H), 4.85 – 4.81 (m, 1H), 4.68 (d, *J* = 6.6, Hz, 1H), 4.66 (d, *J* =

6.6, Hz, 1H), 4.63 (d, *J* = 6.8, Hz, 1H), 4.51 (d, *J* = 6.8 Hz, 1H), 4.34 – 4.23 (m, 3H), 3.84 – 3.76 (m, 1H), 3.76 – 3.68 (m, 1H), 3.62 – 3.54 (m, 1H), 3.37 (s, 3H), 3.31 (s, 3H), 2.64 (dd, *J* = 15.4, 5.6 Hz, 1H), 2.33 – 2.24 (m, 1H), 2.22 (t, *J*= 5.6 Hz, 2H), 1.89 – 1.67 (m, 4H), 1.67 – 1.63 (d, *J* = 5.8 Hz, 3H), 1.62 – 1.49 (m, 2H), 1.05 (s, 9H); $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$) δ 151.4, 135.5, 133.93, 133.89,133.0, 132.0, 129.6, 127.6, 126.9, 104.4, 95.4, 93.9, 81.1, 78.2, 77.2, 72.9, 60.2, 55.5, 55.4, 40.1, 38.5, 37.6, 31.2, 29.9, 26.8, 19.2, 18.0; MS (ESI-TOF) *m/z*: 645 $[M+Na]^+$. HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{37}H_{54}O_6NaSi$: 645.3587; found: 645.3589.

(*S*,*E*)-3-(Methoxymethoxy)-5-((2*R*,5*R*)-5-((*S*,*E*)-3-(methoxymethoxy)hept-5-en-1-yl)-4-methylenetetrahydrofuran-2-yl)pent-4-en-1-ol 30: To a solution of compound **48** (56 mg, 0.09 mmol) in anhydrous THF (2 mL) was added TBAF (1 M in THF, 0.18 mL, 0.18 mmol) at 0 °C and the reaction mixture was stirred for 2 h. The solvent was removed under reduced pressure and the residue was purified by flash chromatography using 10-30% EtOAc/Hexane (v/v) as the eluent to afford primary alcohol **30** (33.52 mg, 0.087 mmol) in 98% yield as a colorless oil.

(*S*)-3-(4-Methoxybenzyloxy)-2-methylpropanal 49[24]: To a solution of alcohol (2.1 g, 10 mmol) in anhydrous CH_2Cl_2 (40 mL) was added Dess-Martin periodinane (6.36 g, 15 mmol). After being stirred at rt for 30 min, the reaction mixture was quenched with aq satd $Na_2S_2O_3$ (5 mL) and aq satd $NaHCO_3$ solution (5 mL). The aq phase was extracted with CH_2Cl_2 (3x30 mL). The combined organic extracts were washed with water (40 mL), brine (40 mL) dried over anhydrous Na_2SO_4 and concentrated in vacuo. The residue was purified by flash column chromatography on silica gel using 10% EtOAc/Hexane (v/v) as the eluent to afford compound **49** (1.91 g, 9.2 mmol) in 92% yield as a liquid. TLC: R_f 0.3 (10% EtOAc/Hexane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.71 (d, *J* = 1.6 Hz, 1H), 7.24 (d, *J* = 8.7 Hz, 2H), 6.88 (d, *J* = 8.7 Hz, 2H), 4.45 (s, 2H), 3.80 (s, 3H), 3.65 (dd, *J* = 9.4, 6.7 Hz, 1H), 3.60 (dd, *J* = 9.4, 5.3

Hz, 1H), 2.69 – 2.60 (m, 1H), 1.12 (d, *J* = 7.1 Hz, 3H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 203.9, 159.2, 129.9, 129.2, 113.8, 72.9, 69.7, 55.2, 46.7, 10.7.

(2*S*,3*S*,4*S*)-1-((4-Methoxybenzyl)oxy)-2,4-dimethylhept-5-yn-3-ol 51: To a solution of $Pd(PPh_3)_2Cl_2$ (280 mg, 0.4 mmol) in anhydrous THF (60 mL) cooled at 0 °C was added the solution of the mesylate **6** (2.6 g, 16 mmol) in anhydrous THF (10 mL) followed by the solution of freshly prepared aldehyde **49** (1.66 g, 8 mmol) in anhydrous THF (10 mL). A solution of Et_2Zn (1 M in Hexane 42 mL, 42 mmol) was added dropwise over period of 10 min and the reaction mixture was allowed to warm to rt over 1 h. Stirring was continued for an additional 1 h . The reaction mixture was cooled to 0 °C and quenched by adding to aq HCl (10%, 30 mL, caution evolution of ethane gas) and diluted with Et_2O (50 mL). The layers were separated and the aq layer extracted with Et_2O (3x60 mL). The combined extracts were washed with water (100 mL), brine (50 mL) and dried over Na_2SO_4. The solvent was removed under reduced pressure and the residue was chromatographed on silica gel using 10% EtOAc/Hexane (v/v) as the eluent to furnish alcohol **51** (1.65 g, 6 mmol) in 75% yield (dr 95:5). TLC: R_f 0.3 (10% EtOAc/Hexane); $[\alpha]^{20}_{D}$ +9.9 (*c* 0.5, $CHCl_3$); IR (Neat) 3480, 2964, 2864, 1612, 1512, 1440, 1247, 1175, 1034, 820, 717 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.18 (d, *J* = 8.2 Hz, 2H), 6.80 (d, *J* = 8.2 Hz, 2H), 4.45 (d, *J* = 11.6 Hz, 1H), 4.42 (d, *J* = 11.6 Hz, 1H), 3.74 (s, 3H), 3.52 (dd, *J* = 9.1, 6.1 Hz, 1H), 3.48 – 3.44 (m, 1H), 3.42 (dd, *J* = 9.1, 5.5 Hz, 1H), 2.61 – 2.45 (m, 1H), 2.25 (d, *J* = 5.1 Hz, 1H), 1.99 – 1.89 (m, 1H), 1.74 (d, *J* = 2.3 Hz, 3H), 1.07 (d, *J* = 7.0 Hz, 3H), 0.89 (d, *J* = 7.0 Hz, 3H); $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$) δ 159.1, 130.5, 129.1, 113.8, 80.5, 78.2, 75.8, 73.6, 72.8, 55.2, 36.2, 30.7, 18.1, 10.9, 3.6; MS (ESI-TOF) *m/z*: 299 $[M+Na]^+$. HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ $C_{17}H_{24}O_3Na$: 299.1623; found: 299.1618.

(2*S*,3*S*,4*S*)-1-((4-Methoxybenzyl)oxy)-2,4-dimethylhept-5-yn-3-yl methanesulfonate 53: To a solution of alcohol **51** (1.5 g, 5.5 mmol) in anhydrous CH_2Cl_2 (10 mL) cooled to 0 °C

was added Et_3N (1.9 mL, 13.8 mmol) and Ms-Cl (0.65 mL, 8.5 mmol). The reaction mixture was stirred at the same temperature for 30 min before it was quenched by the addition of satd aq $NaHCO_3$ (20 mL) at 0 °C. After the mixture was warmed to 25 °C, the organic layer was separated and the aq layer was extracted with CH_2Cl_2 (2x20 mL). The combined organic extracts were washed with water (20 mL), brine (50 mL) and were dried over Na_2SO_4. Filtration and concentration afforded the mesylate **53** (1.85 g, 5.22 mmol) in 95% yield as pale yellow oil, which was used in the next step without further purification. TLC: R_f 0.2 (10%EtOAc/Hexane); $[\alpha]^{20}_D$ +5.7 (*c* 0.5, $CHCl_3$); IR (Neat) 2938, 2861, 1612, 1513, 1247, 1174, 1088, 1034, 923, 829 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.26 (d, *J* = 8.7 Hz, 2H), 6.87 (d, *J* = 8.7 Hz, 2H), 4.62 (dd, *J* = 7.4, 4.4 Hz, 1H), 4.47 (d, *J* = 11.4 Hz, 1H), 4.39 (d, *J* = 11.4 Hz, 1H), 3.80 (s, 3H), 3.51 (dd, *J* = 9.3, 4.6 Hz, 1H), 3.45 (dd, *J* = 9.3, 5.4 Hz, 1H), 3.05 (s, 3H), 2.93 – 2.86 (m, 1H), 2.34 – 2.25 (m, 1H), 1.78 (d, *J* = 2.4 Hz, 3H), 1.26 (d, *J* = 7.0 Hz, 3H), 1.09 (d, *J* = 7.0 Hz, 3H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 159.1, 130.4, 129.2, 113.7, 87.0, 78.7, 78.3, 72.8, 71.2, 55.2, 38.6, 36.5, 29.2, 18.5, 14.8, 3.5; MS (ESI-TOF) *m/z*: = 377 $[M+Na]^+$. HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{18}H_{26}O_5NaS$: 377.1393; found: 377.1410.

1-((((2*R*,4*R*)-2,4-Dimethylhept-5-yn-1-yl)oxy)methyl)-4-methoxybenzene 55: To the suspension of LAH (874 mg, 23 mmol) in anhydrous Et_2O (40 mL) cooled at 0 °C was added the solution of mesylate **53** (1.6 g, 4.5 mmol) in Et_2O (10 mL). The reaction mixture was heated under reflux for 1 h. The reaction mixture was then cooled to 0 °C, diluted with Et_2O (40 mL) and quenched with small pieces of ice. The gel that separated out was filtered, the filter cake washed with EtOAc (2x50 mL) and the combined filtrate evaporated under reduced pressure. The crude product was purified by flash chromatography on silica gel using hexane (v/v) as the eluent to afford compound **55** (936 mg, 3.6 mmol) in 80% yield as a colourless oil. TLC: R_f 0.3 (10%EtOAc/Hexane); $[\alpha]^{20}_D$ -15.2 (*c* 0.5, $CHCl_3$); IR (Neat) 2959,

2854, 1612, 1512, 1459, 1247, 1091, 1036, 820 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.25 (d, *J* = 8.6 Hz, 2H), 6.87 (d, *J* = 8.7 Hz, 2H), 4.44 (d, *J* = 11.7 Hz, 1H), 4.42 (d, *J* = 11.7 Hz, 1H), 3.8 (s, 3H), 3.34 (dd, *J* = 9.1, 5.2 Hz, 1H), 3.24 (dd, *J* = 9.1, 6.6 Hz, 1H), 2.47 – 2.39 (m, 1H), 2.02 – 1.85 (m, 1H), 1.77 (d, *J* = 2.3 Hz, 3H), 1.41 – 1.32 (m, 1H), 1.27 – 1.17 (m, 1H), 1.1 (d, *J* = 6.8 Hz, 3H), 0.96 (d, *J* = 6.8 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 159.0, 130.9, 129.0, 113.7, 84.0, 75.4, 74.9, 72.6, 55.2, 41.4, 31.4, 23.6, 21.5, 17.8, 3.5; MS (ESI-TOF) *m/z*: 283 $[M+Na]^+$. HRMS (ESI-TOF) *m/z*: $[M+H]^+$ calcd for $C_{17}H_{25}O_2$: 261.1868; found: 261.1849.

1-((((2*R*,4R,*E*)-6-Iodo-2,4-dimethylhept-5-en-1-yl)oxy)methyl)-4-methoxybenzene 4: To solution of Cp_2ZrCl_2 (1.92 g, 6.6 mmol) in anhydrous THF (8 mL) cooled at 0 °C was added DIBAL-H (1.2 M in toluene, 5.5 mL, 6.6 mmol). The reaction mixture was stirred at the same temperature for 30 min. To the above, the solution of alkyne **55** (0.86 g, 3.3 mmol) in anhydrous THF (4 mL) was added. The reaction mixture was warmed to rt and stirring continued until a homogenous solution resulted 1 h. The reaction mixture was cooled to -78 °C and a solution of I_2 (1.7 g, 6.6 mmol) in anhydrous THF (4 mL) was added. Stirring was continued at -78 °C for 30 min and the reaction mixture was quenched with aq 1 N HCl (10 mL). The layers were separated and the aq layer was extracted with EtOAc (3x20 mL). The combined organic layer were washed with aq satd $Na_2S_2O_3$ (30 mL), aq satd $NaHCO_3$ (30 mL), water (30 mL), brine (30 mL) and dried over Na_2SO_4. Evaporation of the solvent afforded the crude iodo compound which was purified by flash column chromatography using hexane as the eluent to afford pure product **4** (1.06 g, 2.73 mmol) in 83% yield as a colourless liquid. TLC: R_f 0.2 (hexane); $[\alpha]^{20}_D$ -41.2 (*c* 1, $CHCl_3$); IR (Neat) 2959, 2854, 1612, 1512, 1459, 1247, 1091, 1036, 820 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.25 (d, *J* = 8.2 Hz, 3H), 6.88 (d, *J* = 8.7 Hz, 2H), 5.94 (dq, *J* = 9.8, 1.5 Hz, 1H), 4.44 (d, *J* = 11.7 Hz, 1H), 4.40 (d, *J* = 11.7 Hz, 1H), 3.81 (s, 3H), 3.26 (dd, *J* = 9.0, 5.5 Hz, 1H), 3.18 (dd, *J* = 9.0,

6.5 Hz, 1H), 2.54 – 2.40 (m, 1H), 2.31 (d, *J* = 1.5 Hz, 3H), 1.80 – 1.69 (m, 1H), 1.40 – 1.34 (m, 1H), 1.14 – 1.04 (m, 1H), 0.92 (d, *J* = 6.7 Hz, 3H), 0.91 (d, *J* = 6.6 Hz, 3H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 159.1, 147.6, 130.7, 129.1, 113.7, 92.3, 75.1, 72.6, 55.3, 40.9, 33.2, 31.2, 27.6, 20.3, 17.7; MS (ESI-TOF) *m/z*: = 411 $[M+Na]^+$.

(1*E*,3*S*,6*E*,8*R*,10*R*)-11-((4-Methoxybenzyl)oxy)-3-(methoxymethoxy)-1-((2*R*,5*R*)-5-((*S*,*E*)-3-(methoxymethoxy)hept-5-en-1-yl)-4-methylenetetrahydrofuran-2-yl)-6,8,10-trimethylundeca-1,6-dien-5-ol 58: To a stirred suspension of $NiCl_2$ (2.2 mg, 0.017 mmol) and $CrCl_2$ (215 mg, 1.75 mmol) in a degassed mixture of THF:DMF (4:1, 1 mL, freeze-pump thaw cycles) cooled at 0 °C under an argon atmosphere was added the solution of the aldehyde **3** (26.7 mg, 70 μmol) and alkenyl iodide **4** (68 mg, 0.175 mmol) in THF:DMF (4:1, 1 mL). The mixture was stirred for 12 h, then quenched with satd aq NH_4Cl and diluted with EtOAc (5 mL). The layers were separated and the aq layer was extracted with EtOAc (3x10 mL). The combined organic layers were washed with water (10 mL), brine (10 mL), dried over Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by flash chromatography on silica gel 10-20% EtOAc/Hexane (v/v) as the eluent to give alcohol **57** (36 mg, 56 μmol) in 81% yield as a pale yellow oil. TLC: R_f 0.2 (20% EtOAc/Hexane); IR (Neat) 3446, 2927, 1616, 1516, 1458, 1372, 1250, 1154, 1097, 1039, 975, 918, 821 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.25 (d, *J* = 8.7 Hz, 2H), 6.87 (d, *J* = 8.7 Hz, 2H), 5.75 (dd, *J* = 15.5, 6.5 Hz, 1H), 5.65 (dd, *J* = 15.6, 6.9 Hz, 1H), 5.54 – 5.35 (m, 2H), 5.21 (d, *J* = 9.2 Hz, 1H), 4.96 (s, 1H), 4.83 (s, 1H), 4.72 (d, *J* = 6.8 Hz, 1H), 4.65 (d, *J* = 6.8 Hz, 2H), 4.52 (d, *J* = 6.8 Hz, 1H), 4.43 (d, *J* = 11.7 Hz, 1H), 4.39 (d, *J* = 11.9 Hz, 1H), 4.35 – 4.21 (m, 3H), 4.20 – 4.10 (m, 1H), 3.80 (s, 3H), 3.62 – 3.54 (m, 1H), 3.39 (s, 3H), 3.37 (s, 3H), 3.31 – 3.25 (m, 1H), 3.20 – 3.13 (m, 1H), 2.67 (dd, *J* = 15.2, 4.1 Hz, 1H), 2.48 – 2.38 (m, 1H), 2.36 – 2.28 (m, 2H), 2.21 (t, *J* = 6.6 Hz, 2H), 1.90 – 1.78 (m, 2H), 1.76 – 1.66 (m, 3H), 1.65 (d, *J* = 5.8 Hz, 3H), 1.64 – 1.59 (m, 1H), 1.57 (d, *J* = 0.8 Hz, 3H), 1.39 – 1.31 (m, 1H), 1.10 – 1.00 (m,

1H), 0.91 (d, *J* = 6.9 Hz, 3H), 0.88 (d, *J* = 7.9 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 159.0, 151.1, 135.0, 134.9, 134.0, 133.0*, 132.9, 132.6*, 131.7, 131.3*, 130.9, 129.1, 127.69, 127.0, 113.7, 104.6, 95.3, 94.31, 93.55*, 81.2, 81.1*, 78.2, 78.1*, 77.24, 77.21*, 76.2, 76.1*, 75.5, 75.4*, 74.0, 73.3*, 72.6, 55.8, 55.7*, 55.5, 55.3, 41.4, 40.1, 37.6, 31.9, 31.3, 31.2, 31.1*, 30.91, 30.87*, 29.4, 20.7, 18.1, 17.8, 12.0, 11.7*; MS (ESI-TOF) *m/z*: 667 $[M+Na]^+$. HRMS (ESI): *m/z*: $[M+Na]^+$ calcd for $C_{38}H_{60}O_8Na$: 667.4186; found: 667.4192. **Note**: The signals marked with an asterisk mark correspond to the epimeric alcohol.

(1*E*,3*S*,6*E*,8*R*,10*R*)-11-((4-Methoxybenzyl)oxy)-3-(methoxymethoxy)-1-((2*R*,5*R*)-5-((*S*,*E*)-3-(methoxymethoxy)hept-5-en-1-yl)-4-methylenetetrahydrofuran-2-yl)-6,8,10-trimethylundeca-1,6-dien-5-one 60: Following the procedure detailed for the preparation of aldehyde **3** from alcohol **30**, alcohol **58** (120 mg, 0.045 mmol) was treated with Dess−Martin periodinane (13 mg, 0.03 mmol) in anhydrous dichloromethane to afford compound **60** (24.4 mg, 0.038 mmol) in 84% yield as a colorless oil. TLC: R_f 0.3 (15% EtOAc/Hexane); $[\alpha]^{20}_D$ -15 (*c* 0.3, $CHCl_3$); IR (Neat) 2929, 2858, 1672, 1622, 1454, 1376, 1252, 1099, 1040, 975, 756 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.24 (d, *J* = 8.7 Hz, 2H), 6.88 (d, *J* = 8.7 Hz, 2H), 6.38 (d, *J* = 9.6 Hz, 1H), 5.79 (dd, *J* = 15.5, 6.4 Hz, 1H), 5.67 (dd, *J* = 15.5, 7.2 Hz, 1H), 5.54 – 5.38 (m, 2H), 4.99 – 4.93 (m, 1H), 4.85 – 4.80 (m, 1H), 4.68 (d, *J* = 6.8 Hz, 1H), 4.64 (d, *J* = 6.8 Hz, 2H), 4.62 – 4.59 (m, 1H), 4.53 (d, *J* = 6.7 Hz, 1H), 4.44 (d, *J* = 11.7 Hz, 1H), 4.39 (d, *J* = 11.7 Hz, 1H), 4.35 – 4.22 (m, 2H), 3.63 – 3.54 (m, 1H), 3.37 (s, 3H), 3.31 (s, 3H), 3.25 (dd, *J* = 9.0, 5.6 Hz, 1H), 3.20 (dd, *J* = 9.0, 6.3 Hz, 1H), 3.09 (dd, *J* = 16.0, 8.5 Hz, 1H), 2.74 – 2.57 (m, 3H), 2.37 – 2.27 (m, 2H), 2.22 (t, *J*= 5.7 Hz, 2H), 1.91 – 1.75 (m, 2H), 1.73 (d, *J*= 6.0 Hz, 3H), 1.66 (dd, *J* = 6.0, 1.1 Hz, 3H), 1.63 – 1.54 (m, 2H), 1.53 – 1.46 (m, 1H), 1.20 – 1.11 (m, 1H), 0.98 (d, *J* = 6.6 Hz, 3H), 0.93 (d, *J* = 6.7 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 199.0, 159.1, 151.2, 149.3, 135.7, 133.1, 131.4, 130.7, 129.1, 127.7, 126.9, 113.7, 104.5, 95.3, 94.1, 81.1, 78.1, 77.2, 75.1, 72.71, 72.67, 55.6, 55.6, 55.3, 43.2, 40.8,

40.1, 37.6, 31.9, 31.4, 31.2, 29.4, 19.8, 18.1, 17.7, 11.4; MS (ESI-TOF) *m/z*: 665 $[M+Na]^+$. HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{38}H_{58}O_8Na$: 665.4029; found: 665.4037.

(2*R*,5*R*)-5-((1*E*,3*S*,6*E*,8*R*,10*R*)-11-((4-Methoxybenzyl)oxy)-3-(methoxymethoxy)-6,8,10-trimethyl-5-methyleneundeca-1,6-dien-1-yl)-2-((*S*,*E*)-3-(methoxymethoxy)hept-5-en-1-yl)-3-methylenetetrahydrofuran 62: To a suspension of methyltriphenylphosphonium bromide (10.6 mg, 0.014 mmol) in dry THF (2 mL) was treated with *n*-BuLi (2.5 M solution in hexane, 56 µL, 0.14 mmol,) under N_2 at 0 °C. The resulting yellow solution was allowed to stir at rt for 30 min. To the keto compound **60** (20 mg, 0.03 mmol) in anhydrous THF (0.5 mL) maintained at -30 °C the above prepared ylide was added. The reaction mixture was stirred at -30 °C for 15 min and then quenched with H_2O (2 mL). The mixture was extracted with EtOAc (3x5 mL). The combined organic extracts were washed with water (5 mL), brine (5 mL), dried over anhydrous Na_2SO_4, filtered and concentrated. The residue was purified by silica gel column chromatography using 3-5% EtOAc/Hexane (v/v) as the eluent to afford the pure compound **62** (14.4 mg, 0.022 mmol) in 75% yield as a colourless oil. TLC: R_f 0.3 (10% EtOAc/Hexane); $[\alpha]^{20}_D$ -12 (*c* 0.3, $CHCl_3$); IR (Neat) 2897, 2114, 1622,1512, 1247, 1030, 820, 505 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.25 (d, *J* = 8.6 Hz, 2H), 6.87 (d, *J* = 8.6 Hz, 2H), 5.67 (dd, *J* = 15.5, 6.2 Hz, 1H), 5.59 (dd, *J* = 15.5, 6.9 Hz, 1H), 5.55 – 5.40 (m, 2H), 5.36 (d, *J* = 9.2 Hz, 1H), 5.04 (d, *J* = 1.3 Hz, 1H), 4.95 (d, *J* = 1.3 Hz, 1H), 4.91 (s, 1H), 4.82 (s, 1H), 4.67 (d, *J* = 6.8 Hz, 1H), 4.64 (d, *J* = 6.8 Hz, 2H), 4.49 (d, *J* = 6.7 Hz, 1H), 4.44 (d, *J* = 11.9 Hz, 1H), 4.40 (d, *J* = 11.9 Hz, 1H), 4.33 – 4.23 (m, 2H), 4.22 – 4.11 (m, 1H), 3.80 (s, 3H), 3.62 – 3.54 (m, 1H), 3.37 (s, 3H), 3.31 (s, 3H), 3.28 (dd, *J* = 9.0, 5.3 Hz, 1H), 3.18 (dd, *J* = 9.0, 6.9 Hz, 1H), 2.69 – 2.50 (m, 3H), 2.45 (dd, *J* = 14.1, 6.2 Hz, 1H), 2.38 – 2.26 (m, 3H), 2.22 (t, *J* = 5.8 Hz, 2H), 2.08 – 1.97 (m, 1H), 1.88 – 1.76 (m, 2H), 1.73 (s, 3H), 1.66 (d, *J* = 5.8 Hz, 3H), 1.44 – 1.35 (m, 1H), 1.15 – 1.06 (m, 1H), 0.94 (d, *J* = 6.6 Hz, 6H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 159.1, 151.4, 145.4, 135.0, 132.6, 131.86, 131.85, 130.9, 129.1,

127.6, 127.0, 113.7, 113.0, 104.4, 95.3, 93.9, 81.1, 78.1, 77.2, 75.4, 74.8, 72.6, 55.5, 55.3, 55.3, 41.5, 40.5, 40.2, 37.6, 31.9, 31.4, 31.2, 29.4, 22.7, 18.1, 17.8, 14.4; MS (ESI-TOF) *m/z*: 663 $[M+Na]^+$. HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{39}H_{60}O_7Na$: 663.4237; found: 663.4235.

(*S*)-3-((*tert*-Butyldiphenylsilyl)oxy)-2-methylpropanal 50[24]**:** Following the procedure detailed for the preparation of aldehyde **49** from alcohol, aldehyde **50** (3.9 g, 11.96 mmol) was obtained in 92% yield as a viscous oil. TLC: R_f 0.5 (10% EtOAc/Hexane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.76 (d, *J* = 1.6 Hz, 1H), 7.66 – 7.63 (m, 4H), 7.45 – 7.38 (m, 6H), 3.90 (dd, *J* = 10.3, 4.9 Hz, 1H) 3.83 (dd, *J* = 10.4, 6.4Hz, 1H), 2.65 – 2.50 (m, 1H), 1.11 (d, *J* = 6.9 Hz, 3H), 1.04 (s, 9H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 204.4, 135.6, 133.2, 129.8, 127.7, 64.1, 48.8, 26.8, 19.2, 10.3.

(2*S*,3*S*,4*S*)-1-((*tert*-Butyldiphenylsilyl)oxy)-2,4-dimethylhept-5-yn-3-ol 52: Following the procedure detailed for the preparation of compound **51**, aldehyde **50** (3.58 g, 11 mmol) and mesylate **6** (2.67 g, 16.5 mmol) was treated with $Pd(PPh_3)_2Cl_2$ (245 mg, 0.35 mmol) in anhydrous THF (110 mL) and Et_2Zn (1 M in Hexane, 33 mL, 33 mmol) to furnish alcohol **52** (3.12 g, 7.9 mmol) in 72% yield as a colourless oil. (dr 95:5). TLC: R_f 0.3 (5% EtOAc/Hexane); $[\alpha]^{20}_D$ +8.1 (*c* 0.5, $CHCl_3$); IR (Neat) 3480, 2964, 2864, 1612, 1512, 1440, 1247, 1175, 1034, 820, 717 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.69 – 7.63 (m, 4H), 7.43 – 7.36 (m, 6H), 3.70 (dd, *J* = 10.7, 5.9 Hz, 1H), 3.65 (dd, *J* = 10.7, 4.9 Hz, 1H), 3.57 – 3.53 (m, 1H), 2.66 – 2.57 (m, 1H), 2.30 (bs, 1H), 1.87 – 1.82 (m, 1H), 1.80 (d, *J* = 3.9 Hz, 3H), 1.14 (d, *J* = 7.0 Hz, 3H), 1.1 (s, 9H), 0.94 (d, *J* = 5.6 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 135.6, 133.6, 129.6, 127.6, 80.5, 78.2, 75.7, 67.4, 38.1, 30.8, 26.9, 19.3, 18.1, 10.7, 3.6; MS (ESI-TOF) *m/z*: 417 $[M+Na]^+$. HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{25}H_{34}O_2NaSi$: 417.2226; found: 417.2222.

(2*S*,3*S*,4*S*)-1-((*tert*-Butyldiphenylsilyl)oxy)-2,4-dimethylhept-5-yn-3-yl methanesulfonate 54: Following the procedure detailed for the preparation of compound **53**, alcohol **52** (2.75 g, 7 mmol) was treated with Et_3N (1.95 mL, 14 mmol) and Ms-Cl (0.8 mL, 10.5 mmol) to give mesylate **54** (2.97 g, 6.3 mmol) in 90% yield as a pale yellow oil, which was used in the next step without further purification. TLC: R_f 0.3 (5% EtOAc/Hexane); $[\alpha]^{20}_D$ +10.8 (*c* 1, $CHCl_3$); IR (Neat) 2938, 2861, 1612, 1513, 1247, 1174, 1088, 1034, 923, 829 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.70 – 7.63 (m, 4H), 7.46 – 7.36 (m, 6H), 4.91 – 4.81 (m, 1H), 3.67 (dd, *J* = 10.4, 6.8 Hz, 1H), 3.58 (dd, *J* = 10.4, 5.5 Hz, 1H), 3.05 (s, 3H), 2.88 – 2.82 (m, 1H), 2.21 – 2.10 (m, 1H), 1.74 (d, *J* = 2.3 Hz, 3H), 1.21 (d, *J* = 7.0 Hz, 3H), 1.07 (s, 9H), 0.96 (d, *J* = 6.8 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 135.6, 133.6, 133.4, 129.7, 127.7, 85.8, 79.3, 78.4, 65.6, 38.7, 37.9, 29.8, 26.8, 19.3, 18.2, 12.1, 3.6; MS (ESI-TOF) *m/z*: 495 $[M+Na]^+$. HRMS (ESI-TOF) *m/z*: $[M+H]^+$ calcd for $C_{26}H_{37}O_4SSi$: 473.2182; found: 473.2176.

***tert*-Butyl(((2*R*,4*R*)-2,4-dimethylhept-5-yn-1-yl)oxy)diphenylsilane 56[6]:** Following the procedure detailed for the preparation of compound **55**, mesylate **54** (2.36 g, 5 mmol) was treated with LAH (950 mg, 25 mmol) to afford compound **56** (1.4 g, 3.75 mmol) in 75% yield as a colourless liquid. TLC: R_f 0.6 (2% EtOAc/Hexanes); $[\alpha]^{20}_D$ -13.2 (*c* 0.8, $CHCl_3$); IR (Neat) 2959, 2854, 1612, 1512, 1459, 1247, 1091, 1036, 820 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.68 – 7.64 (m, 4H), 7.43 – 7.37 (m, 6H), 3.57 (dd, *J* = 10.5, 5.6 Hz, 1H), 3.49 (dd, *J* = 10.5, 6.0 Hz, 1H), 2.44 – 2.34 (m, 1H), 1.77 (d, *J* = 2.4 Hz, 3H), 1.60 – 1.53 (m, 1H), 1.49 (dd, *J* = 13.1, 6.8 Hz, 1H), 1.30 – 1.22 (m, 1H), 1.09 (d, *J* = 6.8 Hz, 3H), 1.07 (s, 9H), 0.98 (d, *J* = 6.8 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 135.6, 134.1, 129.5, 127.6, 84.2, 75.4, 68.2, 41.0, 33.7, 26.9, 23.7, 21.6, 19.4, 17.7, 3.5; MS (ESI-TOF) *m/z*: 379 $[M+H]^+$. HRMS (ESI-TOF) *m/z*: $[M+H]^+$ calcd for $C_{25}H_{35}OSi$:379.2457; found: 379.2452.

***tert*-Butyl(((2*R*,4*R*,*E*)-6-iodo-2,4-dimethylhept-5-en-1-yl)oxy)diphenylsilane 57[6]:** Following the procedure detailed for the preparation of compound **4**, alkyne **56** (1.13 g, 3 mmol) furnished iodo alkene **57** (1.14 g, 2.25 mmol) in 75% yield as a colorless liquid. TLC: R_f 0.2 (Hexane); $[\alpha]^{20}_D$ -26.6 (*c* 1.2, $CHCl_3$); IR (Neat) 2959, 2854, 1612, 1512, 1459, 1247, 1091, 1036, 820, 495cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 – 7.64 (m, 4H), 7.44 – 7.36 (m, 6H), 5.92 (dq, *J* = 9.8, 1.6 Hz, 1H), 3.50 (dd, *J* = 9.8, 5.0, Hz, 1H), 3.41 (dd, *J* = 9.8, 6.0, Hz, 1H), 2.42 – 2.34 (m, 1H), 2.22 (d, *J* = 1.5 Hz, 3H), 1.70 – 1.58 (m, 1H), 1.48 – 1.38 (m, 1H), 1.06 (s, 9H), 1.05 – 1.0 (m, 1H) 0.95 (d, *J* = 6.2 Hz, 3H), 0.90 (d, *J* = 5.8 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 147.6, 135.6, 133.9, 129.5, 127.6, 92.3, 68.2, 40.3, 33.4, 33.3, 27.5, 26.9, 20.4, 19.3, 17.5; MS (ESI-TOF) *m/z*: 507 $[M+H]^+$. HRMS (ESI-TOF) *m/z*: $[M+H]^+$ calcd for $C_{25}H_{36}IOSi$: 507.1580; found: 507.1588.

(1*E*,3*S*,6*E*,8*R*,10*R*)-11-((4-Methoxybenzyl)oxy)-3-(methoxymethoxy)-1-((2*R*,5*R*)-5-((*S*,*E*)-3-(methoxymethoxy)hept-5-en-1-yl)-4-methylenetetrahydrofuran-2-yl)-6,8,10-trimethylundeca-1,6-dien-5-ol 59: Following the procedure detailed for the preparation of alcohol **58**, aldehyde **3** (460 mg, 0.71 mmol) and alkenyl iodide **57** (50 mg, 0.1 mmol) afforded alcohol **59** (16 mg, 0.021 mmol) in 73% yield as a colourless oil. TLC: R_f 0.2 (20% EtOAc/Hexane); IR (Neat) 3446, 2927, 1616, 1516, 1458, 1372, 1250, 1154, 1097, 1039, 975, 918, 821, 503 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 – 7.59 (m, 4H), 7.47 – 7.33 (m, 6H), 5.74 (dd, *J* = 15.6, 6.4 Hz, 1H), 5.61 (dd, *J* = 15.6, 7.7 Hz, 1H), 5.53 – 5.37 (m, 2H), 5.18 (d, *J* = 9.5 Hz, 1H), 5.0 – 4.93 (m, 1H), 4.85 – 4.81 (m, 1H), 4.68 (d, *J* = 6.8 Hz,1H), 4.66 (d, *J* = 6.8 Hz,1H), 4.64 (d, *J* = 6.8 Hz,1H), 4.54 (d, *J* = 6.8 Hz, 1H), 4.36 – 4.23 (m, 3H), 4.23 – 4.09 (m, 1H), 3.64 – 3.54 (m, 1H), 3.53 – 3.45 (m, 1H), 3.44 – 3.40 (m, 1H), 3.39 (s, 3H), 3.37 (s, 3H), 2.67 (dd, *J* = 15.4, 5.5 Hz, 1H), 2.41 – 2.27 (m, 3H), 2.21 (t, *J* = 5.4 Hz, 2H), 1.90 – 1.76 (m, 2H), 1.76 – 1.68 (m, 2H), 1.65 (dd, *J* = 5.7, 1.1 Hz, 3H), 1.64 – 1.52 (m, 2H), 1.50 (s, 3H), 1.42 (ddd, *J* = 18.5, 9.3, 4.3 Hz, 1H), 1.05 (s, 9H), 1.02 – 0.96 (m, 1H),

0.94 (d, *J* = 6.6 Hz, 3H), 0.87 (d, *J* = 6.7 Hz, 3H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 151.2, 151.1*, 135.6, 135.0, 134.9*, 134.0, 132.9*, 132.8, 132.63, 131.7, 131.3*, 129.5, 127.6, 127.5, 126.9, 104.6, 104.5*, 95.3, 94.3, 93.5*, 81.12, 81.05*, 78.1, 78.0*, 77.2, 76.2, 76.1*, 73.9, 73.3*, 68.5, 68.4*, 55.8, 55.6, 55.5*, 41.2, 41.0*, 40.9, 40.1, 37.6, 33.4, 31.2, 31.1*, 29.8, 29.4*, 26.9, 20.8, 19.3, 18.0, 17.6, 12.0, 11.7*; MS (ESI-TOF) *m/z*: 785 $[M+Na]^+$. HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{46}H_{70}O_7NaSi$: 785.4789; found: 785.4779. **Note**: The signals indicated by an asterisk mark compound to the epimeric carbinol.

(1*E*,3*S*,6*E*,8*R*,10*R*)-11-((4-Methoxybenzyl)oxy)-3-(methoxymethoxy)-1-((2*R*,5*R*)-5-((*S*,*E*)-3-(methoxymethoxy)hept-5-en-1-yl)-4-methylenetetrahydrofuran-2-yl)-6,8,10-trimethylundeca-1,6-dien-5-one 61: Following the procedure detailed for the preparation of aldehyde **3** alcohol **59** (15 mg, 20 μmol) on oxidation using Dess−Martin periodinane (13 mg, 0.03 mmol) furnished ketone **61** (11.4 mg, 15 μmol) in 78% yield as a colorless oil. TLC: R_f 0.2 (10% EtOAc/Hexane); $[\alpha]^{20}_D$ -17.8 (*c* 0.75, $CHCl_3$); IR (Neat) 2929, 2858, 1672, 1612, 1454, 1376, 1252, 1099, 1040, 975, 756 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70 – 7.61 (m, 4H), 7.46 – 7.33 (m, 6H), 6.34 (d, *J* = 9.5 Hz, 1H), 5.79 (dd, *J* = 15.6, 6.5 Hz, 1H), 5.73 – 5.63 (dd, *J* = 15.6, 7.3 Hz, 1H), 5.56 – 5.37 (m, 2H), 4.98 – 4.92 (m, 1H), 4.85 – 4.81 (m, 1H), 4.68 (d, *J* = 6.6 Hz,1H), 4.66 (d, *J* = 6.8 Hz,1H), 4.64 (d, *J* = 6.8 Hz,1H), 4.63 – 4.58 (m, 1H) 4.53 (d, *J* = 6.6 Hz, 1H), 4.32 – 4.24 (m, 2H), 3.62 –3.54 (m, 1H), 3.48 (dd, *J* = 9.8, 4.9 Hz, 1H), 3.42 (dd, *J* = 9.8, 5.9 Hz, 1H), 3.37 (s, 3H), 3.30 (s, 3H), 3.1 (dd, *J* = 16.0, 8.6 Hz, 1H), 2.73 – 2.60 (m, 2H), 2.59 – 2.51 (m, 1H), 2.38 – 2.27 (m, 1H), 2.22 (t, *J* = 5.6 Hz, 2H), 1.88 – 1.78 (m, 1H), 1.75 – 1.68 (m, 1H),1.67 – 1.64 (m, 6H)1.63 – 1.47 (m, 4H), 1.17 – 1.08 (m, 1H), 1.05 (s, 9H), 0.97 (d, *J* = 6.6 Hz, 3H) 0.95 (d, *J* = 6.6 Hz, 3H); $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$) δ 199.0, 151.2, 149.3, 135.8, 135.6, 133.8, 133.1, 131.4, 129.6, 127.63, 127.58, 126.9, 104.5, 95.3, 94.1, 81.1, 78.1, 77.2, 72.7, 68.2, 55.51, 55.50, 43.2, 40.2, 40.0, 37.6, 33.5, 31.3, 31.2, 29.8, 26.9, 19.9, 19.3, 18.1, 17.5, 11.3; MS (ESI-TOF) *m/z*: 783

$[M+Na]^+$. HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{46}H_{68}O_7NaSi$: 783.4632; found: 783.4610.

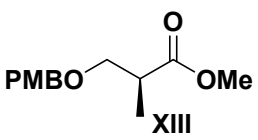
(2*R*,5*R*)-5-((1*E*,3S,6*E*,8*R*,10*R*)-11-((4-Methoxybenzyl)oxy)-3-(methoxymethoxy)-6,8,10-trimethyl-5-methyleneundeca-1,6-dien-1-yl)-2-((*S*,*E*)-3-(methoxymethoxy)hept-5-en-1-yl)-3-methylenetetrahydrofuran 63: Following the procedure detailed for the preparation of compound **62** ketone **61** (10 mg, 0.013 mmol) afforded compound **63** (7.5 mg, 0.0097 mmol) in 75% yield as a colorless oil. TLC: R_f 0.4 (10% EtOAc/Hexane); $[\alpha]^{20}_D$ -15.6 (*c* 0.5, $CHCl_3$); IR (Neat) 2949, 2855, 1615, 1454, 1369, 1252, 1099, 1030, 979, 749 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.70 – 7.61 (m, 4H), 7.46 – 7.33 (m, 6H), 5.67 (dd, *J*= 15.9, 9.7 Hz, 1H), 5.69 (dd, *J* = 15.6, 6.5 Hz, 1H), 5.51 – 5.39 (m, 2H), 5.35 (d, *J* = 9.3 Hz,1H), 5.04 – 5.01 (m, 1H), 4.97 – 4.93 (m, 1H), 4.92 – 4.88 (m, 1H), 4.84 – 4.80 (m, 1H), 4.67 (d, *J* = 6.8, Hz, 1H),4.64 (d, *J* = 6.7, Hz, 1H), 4.63 (d, *J* = 6.8, Hz, 1H), 4.48 (d, *J* = 6.7 Hz, 1H), 4.29 – 4.24 (m, 2H), 4.20 – 4.14 (m, 1H), 3.60– 3.54 (m, 1H), 3.51 (dd, *J* = 9.8, 4.9 Hz, 1H), 3.41 (dd, *J* = 9.8, 6.1 Hz, 1H), 3.37 (s, 3H), 3.31 (s, 3H), 2.68 – 2.55 (m, 3H), 2.51 – 2.40 (m, 2H), 2.33 – 2.26 (m, 1H), 2.22 (t, *J* = 5.6 Hz, 2H), 1.87 – 1.79 (m, 1H), 1.78 – 1.67 (m, 1H), 1.66 (d, *J* = 1.6 Hz, 3H), 1.65 (dd, *J* = 6.1, 1.1 Hz, 3H), 1.64 – 1.58 (m,1H), 1.55 – 1.47 (m, 1H), 1.47 – 1.42 (m, 1H), 1.1 – 0.97 (m, 1H), 1.02 (s, 9H), 0.96 (d, *J* = 6.7 Hz, 3H), 0.92 (d, *J* = 6.6 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 151.4, 145.4, 135.61, 135.58, 135.0, 134.0, 132.6, 131.8, 129.5, 127.63, 127.55, 127.0, 113.0, 104.4, 95.3, 93.8, 81.0, 78.1, 77.2, 74.8, 68.4, 55.5, 55.3, 41.0, 40.5, 40.2, 37.6, 33.6, 31.2, 30.5, 29.8, 26.9, 21.0, 19.3, 18.1, 17.7, 14.4; MS (ESI-TOF) *m/z*: 781 $[M+Na]^+$. HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{47}H_{70}O_6NaSi$: 781.4839; found: 781.4818.

(2*R*,4*R*,5*E*,9*S*,10*E*)-9-(Methoxymethoxy)-11-((2*R*,5*R*)-5-((*S*,*E*)-3-(methoxymethoxy)hept-5-en-1-yl)-4-methylenetetrahydrofuran-2-yl)-2,4,6-trimethyl-7-methyleneundeca-5,10-dien-1-ol 64: To a solution of compound **63** (7.5 mg, 10 μmol) in anhydrous THF (0.4 mL)

was added TBAF (1 M in THF, 20 μL, 0.02 mmol) at 0 °C and the reaction mixture was stirred for 2 h. The solvent was removed under reduced pressure and the residue was purified by flash chromatography using 10-30% EtOAc/Hexane (v/v) as the eluent to obtain primary alcohol **64** (5 mg, 9.8 μmol) in 98% yield as a colourless oil. TLC: R_f 0.2 (20% EtOAc/Hexanes); $[\alpha]^{20}_D$ -14.1 (*c* 0.2, $CHCl_3$); IR (Neat) 3449, 2927, 1621, 1512, 1458, 1374, 1250, 1157, 1097, 1042, 975, 923, 821 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.69 (dd, *J* = 15.5, 6.1 Hz, 1H), 5.59 (dd, *J* = 15.5, 7.0 Hz, 1H), 5.54 – 5.41 (m, 2H), 5.39 (d, *J* = 9.5 Hz, 1H), 5.07 – 5.03 (m, 1H), 4.98 – 4.94 (m, 1H), 4.93 – 4.89 (m, 1H), 4.84 – 4.80 (m, 1H), 4.67 (d, *J* = 6.8 Hz, 1H), 4.65 (d, *J* = 6.7 Hz, 1H), 4.63 (d, *J* = 6.8 Hz, 1H), 4.49 (d, *J* = 6.7 Hz, 1H), 4.33 – 4.25 (m, 2H), 4.23 – 4.12 (m, 1H), 3.62 – 3.55 (m, 1H), 3.52 (dd, *J* = 10.5, 5.2 Hz, 1H), 3.43 – 3.34 (m, 4H), 3.32 (s, 3H), 2.71 – 2.55 (m, 3H), 2.45 (dd, *J* = 14.1, 6.3 Hz, 1H), 2.35 – 2.28 (m, 1H), 2.23 (t, *J* = 5.9 Hz, 2H), 1.87 – 1.81 (m, 1H), 1.79 (d, *J* = 1.0 Hz, 3H), 1.74 – 1.68 (m, 1H), 1.66 (d, *J* = 5.0 Hz, 3H), 1.65 – 1.49 (m, 3H), 1.39 (dd, *J* = 15.3, 6.6 Hz, 1H), 1.15 (dd, *J* = 15.3, 7.7 Hz, 1H), 0.97 (d, *J* = 7.2 Hz, 3H), 0.95 (d, *J* = 7.2 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 151.3, 145.4, 134.8, 132.8, 132.1, 131.8, 127.6, 126.9, 113.2, 104.4, 95.3, 93.8, 81.0, 78.1, 77.2, 74.8, 68.0, 55.5, 55.3, 41.0, 40.6, 40.2, 37.6, 33.6, 31.2, 30.4, 29.8, 20.9, 18.1, 17.2, 14.5; MS (ESI-TOF) *m/z*: 543 $[M+Na]^+$. HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{31}H_{52}O_6Na$: 543.3662; found: 543.3661.

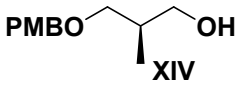
(2*R*,4*R*,5*E*,9*S*,10*E*)-9-(Methoxymethoxy)-11-((2*R*,5*R*)-5-((*S*,*E*)-3-(methoxymethoxy)hept-5-en-1-yl)-4-methylenetetrahydrofuran-2-yl)-2,4,6-trimethyl-7-methyleneundeca-5,10-dienoic acid 65: To a stirred solution of alcohol **64** (5 mg, 9.8 μmol) in CH_2Cl_2 (0.5 mL) were added $NaHCO_3$ (8 mg, 90 μmol) and DMP (9 mg, 19 μmol) at 0 °C and the reaction was allowed to warm to rt and stirred for 1 h. It was quenched with aq $Na_2S_2O_3$ (0.3 mL). The aq layer was extracted with CH_2Cl_2 (3x2 mL) and the combined organic layers were washed with water (2 mL), brine (2 mL) and dried over Na_2SO_4. The solvent was removed under

reduced pressure and the crude aldehyde obtained was dissolved in H_2O/*t*BuOH (1:1, 1 mL) at 0 °C. To the mixture were sequentially added 2-methyl-2-butene (56 μL, 0.5 mmol), NaH_2PO_4 (12 mg, 98 μmol), and $NaClO_2$ (5 mg, 49 μmol). After 15 min, the reaction was warmed to rt. One h later, the reaction was diluted with H_2O (5 mL) and the aq layer was extracted with EtOAc (3x3 mL).The combined organic extracts were washed with brine (5 mL), dried over anhydrous Na_2SO_4, filtered and concentrated. The residue was purified by silica gel column chromatography using 10% $CHCl_3$/methanol (v/v) as the eluent to afford the pure acid compound **65** (3.1 mg, 5.8 μmol) in 60% yield as a viscous oil. TLC: R_f 0.3 (30% EtOAc/Hexanes); $[\alpha]^{20}_D$ -11.3 (*c* 0.1, $CHCl_3$); IR (Neat) 3446, 2927, 1721, 1616, 1516, 1458, 1372, 1250, 1154, 1097, 1039, 975, 918, 821 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.66 (dd, *J* = 15.3, 6.6 Hz, 1H), 5.55 (dd, *J* = 15.3, 7.6 Hz, 1H), 5.51 – 5.38 (m, 2H), 5.33 (d, *J* = 9.1 Hz, 1H), 5.04 (d, *J* = 1.5 Hz, 1H), 4.97 (d, *J* = 1.6 Hz, 1H), 4.90 (d, *J* = 1.5 Hz, 1H), 4.82 (d, *J* = 1.6 Hz, 1H), 4.69 (d, *J* = 6.8 Hz, 1H), 4.67 (d, *J* = 6.8 Hz, 1H), 4.66 (d, *J* = 6.8 Hz, 1H), 4.53 (d, *J* = 6.8 Hz, 1H), 4.35 – 4.26 (m, 2H), 4.23 – 4.13 (m, 1H), 3.64 – 3.56 (m, 1H), 3.38 (s, 3H), 3.34 (s, 3H), 2.75 – 2.59 (m, 3H), 2.56 – 2.46 (m, 1H), 2.42 – 2.28 (m, 3H), 2.22 (t, *J* = 5.7 Hz, 2H), 1.87 – 1.77 (m, 1H), 1.75 (d, *J* = 1.0 Hz, 3H), 1.72 – 1.68 (m, 1H), 1.66 (dd, *J* = 6.0, 1.1 Hz, 3H), 1.63 – 1.49 (m, 2H), 1.48 – 1.41 (m, 1H),1.18 (d, *J* = 7.0 Hz, 3H), 1.1 – 1.05 (m, 1H), 0.99 (d, *J* = 6.5 Hz, 3H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 179.6, 151.3, 145.6, 133.5, 133.4, 133.2, 131.6, 127.7, 126.8, 113.6, 104.5, 95.2, 93.6, 81.0, 78.2, 77.3, 75.0, 55.5, 55.2, 41.4, 40.6, 40.2, 37.6, 37.0, 31.1, 30.8, 29.6, 21.3, 18.1, 17.7, 14.7; MS (ESI-TOF) *m/z*: 557 $[M+Na]^+$. HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{31}H_{50}O_7Na$: 557.3454; found: 557.3461.



XIII

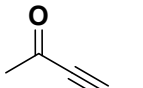
Methyl (*S*)-3-(4-Methoxybenzyloxy)-2-methylpropanoate XIII[24]: A solution of 4-methoxybenzyl alcohol (4.14 g, 30 mmol) in anhydrous Et_2O (60 mL) maintained under N_2 at rt was treated with NaH (60% in oil, 120 mg, 3 mmol). After stirring for 45 min, the solution was cooled to 0 ^oC, trichloroacetonitrile (3 mL, 30 mmol) was added dropwise and the mixture was allowed to warm to rt. The clear solution turned opaque orange. After 2 h, the mixture was concentrated under reduced pressure and hexanes (60 mL) mixed with of methanol (0.4 mL) was added to the mixture. The brown precipitate was removed by filtration and the yellow filtrate was concentrated to a syrup and added to a solution of methyl (*S*)-3-hydroxy-2-methylpropanoate **5** (4.76 g, 20 mmol) in anhydrous CH_2Cl_2 (60 mL). The solution was treated with (D,L)-10-camphorsulfonic acid (0.70 g, 3 mmol) and was stirred for 2 h. The reaction was quenched by the addition of satd aq $NaHCO_3$ (30 mL). The layers were separated and the aq layer was extracted with CH_2Cl_2 (3x40 mL). The combined organic layers were washed with water (30 mL), brine (30 mL), dried over Na_2SO_4 and concentrated. The solid trichloroacetamide formed was removed by filtration with a hexane wash and the filtrate was concentrated to give the crude product which was purified by column chromatography using 10% EtOAc/Hexane (v/v) as the eluent to afford the PMB ether **XIII** (4.66 g, 19.6 mmol) in 98% yield as a colorless oil. TLC: R_f 0.2 (10% EtOAc/Hexane); ^1H NMR (500 MHz,$CDCl_3$) 7.22 (d, J = 8.7 Hz, 2H), 6.84 (d, J = 8.7 Hz, 2H), 4.46 (d, J = 11.7 Hz 1H), 4.44 (d, J = 11.7 Hz 1H), 3.80 (s, 3H), 3.69 (s, 3H), 3.63 (dd, J = 9.0, 7.5 Hz, 1H), 3.46 (dd, J = 9.0, 6.0 Hz, 1H), 2.81–2.72, (m, 1H), 1.17 (d, J = 7.0 Hz, 3H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 175.4, 159.2, 130.3, 129.2, 113.8, 72.8, 71.7, 55.3, 51.7, 40.2, 14.0;



XIV

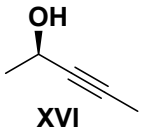
(*R*)-3-((4-Methoxybenzyl)oxy)-2-methylpropan-1-ol XIV[24]: A solution of ester ***I*** (4.8 g, 19 mmol) in anhydrous Et_2O (20 mL) was added slowly to a stirred suspension of LAH (3.6 g, 95 mmol) in Et_2O (40 mL) at 0 ^oC under N_2 atmosphere. After 1 h, the reaction mixture was

allowed to warm to rt and the mixture was stirred for 2 h. The reaction mixture was then cooled to 0 °C, diluted with ether (40 mL) and quenched with small pieces of ice. The gel that separated out was filtered, the filter cake was washed with EtOAc (2x50 mL) and the combined filtrate evaporated under reduced pressure. The crude product was purified by flash chromatography on silica gel using 20% EtOAc/Hexane (v/v) as the eluent to afford alcohol **XIV** (3.87 g, 18.48 mmol) in 97% yield as a colorless oil. TLC: R_f 0.3 (20% EtOAc/Hexane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.24 (d, *J* = 8.7 Hz, 2H), 6.88 (d, *J* = 8.7 Hz, 2H), 3.80 (s, 3H), 3.64 – 3.55 (m, 2H), 3.52 (dd, *J* = 9.1, 4.6 Hz, 1H), 3.39 (dd, *J* = 9.1, 8.1 Hz, 1H), 2.13 – 1.98 (m, 1H), 0.86 (d, *J* = 7.8 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 159.2, 130.1, 129.2, 113.8, 75.0, 73.0, 67.7, 55.2, 35.5, 13.4.



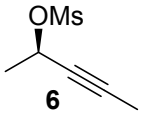
XV

Pent-3-yn-2-one XV[32]**:** A solution of *n*-butyl lithium (2.5 M in Hexane, 40 mL, 100 mmol) was added dropwise during 15 min to a solution of excess of 1-propyne in anhydrous THF (250 mL) cooled to – 78 °C. After 20 min a solution of zinc bromide (1.5 M in THF, 100 mL, 150 mmol) was added. The mixture was warmed to – 40 °C gradually over a period of 20 min. Freshly distilled acetyl chloride (7.2 mL, 100 mmol) was added dropwise over a period of 10 min, the mixture was warmed to 25 °C and stirred for a period of 30 min. The mixture was added to aq satd NH_4Cl (200 mL). After separation of the layers, the aq layer was extracted with Et_2O (3x70 mL). The combined organic layers were washed with water (50 mL), brine (50 mL) and dried over Na_2SO_4. Concentration under reduced pressure afforded the crude productwhich was purified by distillation (bp 70-72 °C/55 mm Hg) to afford the title compound **XV** (6.15 g, 75 mmol) in 75% yield as a colorless oil. TLC: R_f 0.3 (5% EtOAc/Hexane); ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.26 (s, 3H), 1.97 (s, 3H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 184.7, 89.7, 80.6, 32.5, 3.9.



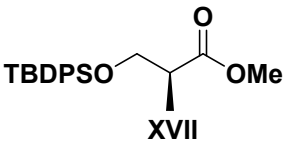
XVI

(*R*)-Pent-3-yn-2-ol XVI[33]**:** Ketone **XV** (5.74 g, 70 mmol) was dissolved in EtOAc (350 mL), sodium formate (47.7 g, 700 mmol), (*R*,*R*)-Noyori catalyst (100 mg, 0.01 mmol), distilled H_2O (350 mL) and hexadecyltrimethylammonium bromide (catalytic amount) were sequentially added. The reaction mixture was stirred at rt for 12 h. The layers were separated and the aq layer was extracted with EtOAc (3x100 mL). The combined organic layers were washed with brine (100 mL), dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by distillation (bp 71-73 ^oC/50mm Hg) to afford the title compound **XVI** (4.11 g, 49 mmol) in 69% yield as a colorless oil. The ratio of enantiomers (95:5) was determined by ^1H NMR analysis of the mandelate esters. TLC: R_f 0.3 (10% EtOAc/Hexane); ^1H NMR (500 MHz, $CDCl_3$) δ 4.53 – 4.45 (m, 1H), 1.84 (d, J = 2.2 Hz, 3H), 1.42 (d, J = 6.6 Hz, 3H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 81.4, 80.0, 58.4, 24.6, 3.4.



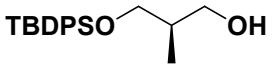
6

(*R*)-3-Pentyn-2-yl methanesulfonate 6[33]**:** Triethylamine (4.3 mL, 30.9 mmol) and methanesulfonyl chloride (1.8 mL, 23.8 mmol) were added successively to a solution of (*R*)-3-pentyn-2-ol **XVI** (1.34 g, 16 mmol) in anhydrous CH_2Cl_2 (80 mL) cooled at –78 °C. The reaction mixture was stirred at the same temperature for 30 min before it was quenched by the addition of satd aq $NaHCO_3$ (20 mL) at –78 °C. The mixture was warmed to 25 °C, the organic layer was separated and the aq layer was extracted with CH_2Cl_2 (2x50 mL). The combined organic extracts were washed with water (50 mL), brine (50 mL) and dried over Na_2SO_4. Filtration and concentration afforded mesylate **6** (2.46 g, 15.2 mmol) as a pale yellow oil in 95% yield which was used in the next step without further purification. TLC: R_f 0.3 (10% EtOAc/Hexane); ^1H NMR (500 MHz, $CDCl_3$) δ 5.32 – 5.22 (m, 1H), 3.10 (s, 3H), 1.89 (d, J = 2.1 Hz, 3H), 1.61 (d, J = 6.6 Hz, 3H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 84.9, 76.0, 68.9, 39.1, 22.9, 3.6.



XVII

(*S*)-Methyl 3-((*tert*-butyldiphenylsilyl)oxy)-2-methylpropanoate XVII[24]: To a solution of compound **5** (2.95 g, 25 mmol) in anhydrous CH_2Cl_2 (50 mL) cooled to 0 °C was added imidazole (3.4 g, 50 mmol) followed by TBDPS-Cl (6.2 mL, 26.2 mmol). The reaction mixture was warmed to rt and stirred for 1 h. The reaction mixture was quenched by the addition of water (50 mL) and diluted with CH_2Cl_2 (50 mL). The layers were separated and the aq layer was extracted with CH_2Cl_2 (3x50 mL). The combined organic layers were washed with water (50 mL), brine (50 mL) and dried over Na_2SO_4. The solvent was evaporated under reduced pressure to afford the crude product which was purified by column chromatography using 5% EtOAc/Hexane (v/v) as the eluent to afford the silyl ether **XVII** (8.72 g, 24.5 mmol) in 98% yield as a gummy oil. TLC: R_f 0.25 (5% EtOAc/Hexane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 – 7.66 (m, 4H), 7.45 – 7.35 (m, 6H), 3.85 (dd, *J* = 9.8, 7.0 Hz, 1H), 3.75 (dd, *J* = 9.8, 5.7 Hz, 1H), 3.68 (s, 3H), 2.77 – 2.67 (m, 1H), 1.17 (d, *J* = 8.5 Hz, 3H), 1.03 (s, 9H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 175.3, 135.5, 133.4, 129.6, 127.6, 65.9, 51.5, 42.4, 26.7, 19.2, 13.4.



XVIII

(*R*)-3-((*tert*-Butyldiphenylsilyl)oxy)-2-methylpropan-1-ol XVIII[24]: To a solution of ester **XVII** (7.87 g, 24 mmol) in anhydrous CH_2Cl_2 (96 mL) cooled to -78 °C was added DIBAL-H (1.2 M in toluene, 44 mL, 52.8 mmol). The reaction mixture was stirred at the same temperature for 1 h and then quenched with aq satd sodium potassium tartarate (50 mL). The reaction mixture was warmed to rt and stirring continued for 1 h. The layers were separated and the aq layer was extracted with CH_2Cl_2 (3x50 mL). The combined organic layers were washed with water (50 mL), brine (50 mL), dried over Na_2SO_4 and concentrated. The residue was purified by column chromatography using 10% EtOAc/Hexane (v/v) as the eluent to

afford pure alcohol **XVIII** (7.63 g, 23.28 mmol) in 97% yield as a colorless liquid. TLC: R_f 0.2 (10% EtOAc/Hexane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 – 7.66 (m, 4H), 7.47 – 7.34 (m, 6H), 3.72 (dd, *J* = 10.1, 4.6 Hz, 1H), 3.66 (dd, *J* = 6.5, 1.3 Hz, 2H), 3.60 (dd, *J* = 10.0, 7.6 Hz, 1H), 2.04 – 1.94 (m, 1H), 1.05 (s, 9H), 0.83 (d, *J* = 6.9 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 135.6, 133.1, 129.8, 127.7, 68.7, 67.6, 37.3, 26.8, 19.1, 13.1.

Supporting Information

^{1}H and ^{13}C NMR spectroscopic characterization data. This material is available free of charge via the internet at http://

Conflict of Interest

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