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The nucleophilic addition of α -metallated 1,3-dioxanes to planar chiral cationic η^3 -allylmolybdenum complexes. Synthesis of (2E,5S,6R,7E)-6-methyl-8-phenylocta-2,7-dienoic acid methyl ester, a key component of the Cryptophycins

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Two adjacent stereogenic centres and a pendant alkene were constructed *via* nucleophilic addition of a 1,3-dioxan-4-ylcopper(I) reagent to a cationic η^3 -allylmolybdenum complex as part of a synthesis of (2*E*,5*S*,6*R*,7*E*)-6-methyl-8-phenylocta-2,7-dienoic acid, a key component of the Cryptophycins. Oxidative addition of Mo(CO)₄(THF)₂ to allyl benzoates provides an efficient synthesis of η^3 -allylmolybdenum(dicarbonyl) complexes.

Introduction

We recently showed that the nucleophilic addition of tetrahydropyran-2-ylcopper(1) reagents to planar chiral η^3 -allylmolybdenum complexes offers a powerful method for the stereoselective appendage of a chain to an oxacyclic ring.¹ The method, illustrated in Scheme 1 for the synthesis of *C*-glycosides,² entails the construction of two adjacent stereogenic centres with a pendant alkene. The high level of stereocontrol is a consequence of the reaction of the organocopper(1) nucleophile with retention of configuration and preferential attack at the allyl ligand *anti* to the molybdenum.³ The one burr under the saddle is the issue of regioselectivity: a combination of steric and electronic factors governs the site of attack. In the case of complex **2**, the steric effect predominates ($\geq 15 : 1$).⁴



We now show that 1,3-dioxan-4-ylcopper(I) reagents are effective nucleophilic partners in the reaction providing a method for the stereoselective appendage of 1,3-diol chains.⁵ The strategy is exemplified for the synthesis of the methyl ester (5) of (2E,5S,6R,7E)-6-methyl-8-phenylocta-2,7-dienoic acid, a key component of the Cryptophycins (Scheme 2).⁶⁻¹⁰ The Cryptophycins are cyclodepsipeptides with pronounced anti-tumour activity owing to their inhibition of tubulin polymerisation.^{11,12} Our synthesis of **5** is a vehicle for exploring the effect of a conjugating substituent on the regioselectivity of nucleophilic addition to η^3 -allylmolybdenum complex **7** using the *a*-metallated dioxane **8** as the nucleophile leading to the dioxane derivative **6** which fixes the *anti* stereochemistry between C5 and C6 in the target.



Cryptophycin 4 (4)



Results and discussion

Synthesis of the cationic η^3 -allylmolybdenum complex 7

The first practical and general synthesis of cationic η^3 -allylmolybdenum complexes (Scheme 3) was reported in 1988 by Faller and Linebarrier^{13,14} who showed that the scalemic allylic acetate **9** derived from Sharpless kinetic resolution of the corresponding allylic alcohol, underwent oxidative addition of the complex Mo(CO)₃(MeCN)₃¹⁵ with retention of configuration to give the neutral complex **10** after reaction with lithium cyclopentadienide. Activation of the planar chiral neutral



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complex with nitrosonium tetrafluoroborate gave the cationic complex 2 as a mixture of diastereoisomers owing to the stereorandom nature of the ligand exchange.

The Faller protocol was substantially modified for the synthesis of the complex 7 (Scheme 4). Easy and efficient kinetic resolution of the racemic allylic alcohol (RS)-11 was accomplished using Novozyme 435, a recombinant immobilised B-component lipase from Candida antarctica, and vinyl acetate, to give (S)-11 and the acetate ester (R)-12 in 45% and 46% yield respectively.^{16,17} The enantiomeric ratio of the allylic alcohol (S)-11 was assayed at 97 : 3 by NMR spectroscopic analysis of the corresponding (R)-acetoxyphenylacetic ester 13. Initial attempts to perform oxidative addition on the acetate ester of (S)-11 using Mo(CO)₃(MeCN)₃ were disappointing. The reaction was very slow in refluxing acetonitrile, requiring five days to go to completion, and the isolated yield of the neutral complex 15 was 35% at best after ligand exchange with lithium cyclopentadienide. A parallel study established that the rate of oxidative addition depended on the ester leaving group, with benzoate giving the optimum yield and rate.¹⁸ When benzoate (S)-14 was treated with Me(CO)₃(MeCN)₃ in refluxing acetonitrile, the reaction was complete in just 28 h and the yield of the isolated neutral complex 15 improved to 76%. A further improvement attended the oxidative addition of $Mo(CO)_4(Py)_2^{19,20}$ to the benzoate ester (S)-14 in refluxing THF: the reaction was complete in 18 h and the yield of the neutral complex 15 climbed to 88%. The neutral complex 15 was obtained as fine yellow needles (mp 85-88 °C) after recrystallisation from ether-pentane but ⁹⁵Mo NMR spectroscopic analysis revealed the presence of exo and endo isomers (exo : endo = 13 : 1) that were easily distinguished by the large difference in chemical shifts.²¹ Finally, ligand exchange with nitrosonium tetrafluoroborate in acetonitrile at 0 °C gave initially two isomeric cationic complexes 7 (ca. 1 : 1) owing to the stereorandom introduction of central chirality at molybdenum. Although the cationic complex 7 could be isolated as a solid by precipitation, it was usually generated and used in solution without purification.



The dramatic improvement in speed and yield observed with $Mo(CO)_4(Py)_2$ and the allyl benzoate begged the question as to whether further improvements could be wrested from ligand substitutions on the molybdenum reagent. $Mo(CO)_4(Py)_2$ was easily synthesised by refluxing $Mo(CO)_6$ in THF for 12 h in the presence of 2 equivalents of pyridine.¹⁹ When the reaction was followed by ⁹⁵Mo NMR spectroscopy, a complex mixture

of Mo species was observed in time dependent ratio which included Mo(CO)₅(THF) and cis-Mo(CO)₄(THF)₂. A clearer picture emerged when Mo(CO)₆ was heated in degassed THF (0.08 M) for 22 h in the absence of pyridine and the reaction was followed by ⁹⁵Mo NMR and IR spectroscopy (Scheme 5). A compound with a signal at -1291 ppm with infrared absorptions at 2077, 1941 and 1893 cm⁻¹ was rapidly formed which we ascribed to Mo(CO)₅(THF). This signal gradually disappeared and was replaced by a major signal at -927 ppm with $\Delta \omega_{1/2} =$ 120 Hz (in THF) due to cis-Mo(CO)₄(THF)₂ and a minor component (ca. 4%) with a signal at -750 ppm, $\Delta\omega_{1/2} = 65$ Hz and IR absorptions at 1919 and 1781 cm⁻¹ which we ascribed to fac-Mo(CO)₃(THF)₃.²² The stereochemistry of cis-Mo(CO)₄-(THF)₂ was assigned from the infrared signals at 2021, 1939, 1893 and 1834 cm⁻¹ and its rapid and quantitative transformation to cis-Mo(CO)₄(PPh₃)₂ on addition of two equivalents of PPh₃.^{23,24} cis-Mo(CO)₄(THF)₂ was stable in THF, in the absence of light and oxygen, and could be precipitated from pentane at -100 °C as a yellow solid but it was too labile to be isolated and characterised by X-ray crystallography.



A mixture of benzoate (S)-14 and $Mo(CO)_4(THF)_2$ was refluxed in THF for 14 h whereupon TLC analysis indicated complete consumption of the benzoate. On addition of LiCp, the neutral complex 15 was obtained in 88% yield.²⁵ Hence the THF complex reacted slightly faster than its pyridine analogue though the yield in this case was identical. In order to explore the scope and synthetic advantages of the novel Mo(CO)₄-(THF)₂ complex, we prepared a series of η^3 -allylmolybdenum complexes 17a-h from allylic benzoates 16a-h using Mo(CO)₄-(Py), (Procedure A) and Mo(CO)₄(THF), (Procedure B) under identical conditions. The data presented in Table 1 shows that the Mo(CO)₄(THF)₂ reagent gave faster reactions though the yields were only marginally better (4-12%). TLC analysis of the progress of the reaction also indicated that the Mo(CO)₄-(THF)₂ reagent gave cleaner reactions, especially in the synthesis of trisubstituted systems such as 17e and 17f.

Synthesis of the 1,3-dioxan-4-ylcopper(1) reagent 8

We planned to generate the key 1,3-dioxan-4-ylcopper(I) reagent by transmetallation of the corresponding stannane to its lithium derivative followed by a second transmetallation to the copper reagent using a Cu(I) salt. The isopropylidene protected 1,3-dioxan-4-ylstannane **25** (Scheme 6) was our initial choice of stereodefined tin precursor because a six-step synthesis from dimethyl (S)-malate had been reported.²⁶ We were unable to implement the published procedure or any of its subsequent renditions²⁷⁻²⁹ but a reliable variation was eventually found and is summarised in Scheme 6. The sequence began with the selective reduction of dimethyl (S)-malate with BH₃.

Table 1 The oxidative addition of Mo(CO)₂(Py)₂ and Mo(CO)₄(THF)₂ to allylic benzoates

		R ³	R ² R ⁴ OBz	A: Mo THF, H B: Mo THF,	$(CO)_4(Py)$ Δ ; then Lic $(CO)_4(THI)$ Δ ; then Lic	₂ (1.05 equi Cp (1.05 equ F) ₂ (1.05 equ Cp (1.05 equ	v) uiv) R ³ uiv) R uiv) R	$ \begin{array}{c} $	p	
	16a-h					17a-h				
	16	R ¹	R ²	R ³	R⁴	Procedure A		Procedure B		
						Time	Yield 17	Time	Yield 17	
	a	Н	Н	Н	Н	12 h	86%	9 h	86%	
	b	Н	Me	Η	Н	20 h	82%	16 h	85%	
	c	Н	Н	Me	Me	56 h	58%	44 h	65%	
	d	Me	Н	CO ₂ Et	Н	72 h	70%	16 h	82%	
	e	Me	Me	Me	Η	59 h	80%	44 h	86%	
	f	Me	Н	Me	Me	82 h	50%	68 h	58%	
	g	Н	Me	iPr	Н			96 h	95%	
	ĥ	Me	Н	CO ₂ Et	Me			24 h	88%	



SMe₂ as described by Moriwake ³⁰ to give the 1,2-diol **18** in 89% yield. The terminal hydroxyl was selectively protected as the triisopropylsilyl (TIPS) ether **19** and the methyl ester was hydrolysed to give carboxylic acid **20**. The hydroxyl and carboxyl groups were protected as the 1,3-dioxan-4-one derivative **21** in 94% yield on treatment of **20** with 2-methoxypropene in the presence of pyridinium *p*-toluenesulfonate (PPTS). Reduction of the dioxanone to the lactol with DiBAL-H at -78 °C followed immediately by *in situ* acetylation with acetic anhydride in the presence of DMAP gave the (4*S*,6*S*)-acetoxydioxane **22** in 84% yield as a single isomer. The high stereoselectivity in the reduction-acetylation sequence was precedented in similar transformations on dioxanones reported by Rychnovsky.^{31,32}

The conversion of the acetoxydioxane **22** to the *O*,*S*-acetal **23a,b** was the most vexatious step in the sequence. Initial

attempts to exploit precedent³² by using thiophenol and BF₃. OEt₂ in dichloromethane at a variety of temperatures and times invariably returned the S, S-acetal 24 as the sole product. Use of PhSSiMe₃ in place of thiophenol gave trace amounts of 23a,b at -78 °C using BF₃·OEt₂ as promoter but the combination of PhSSiMe₃ and ZnCl₂ at -60 °C in dichloromethane gave the desired *O*,*S*-acetals **23a**,**b** (a : b = 1 : 3) in 81% yield after only 5 min. Finally, the best results were obtained by simply treating 22 with thiophenol in the presence of 4 mol% ZnCl₂ at -30 °C for 5 min whereupon 23a,b was obtained in 87% yield (a : b = 9:1) with only a trace of 24 being formed by TLC. The diastereoisomeric acetals 23a,b were separable by column chromatography and their relative stereochemistry was easily determined by the characteristic signals for the acetal methyl groups in the ¹³C NMR spectra. The syn-isomer 23a revealed signals at 30.1 and 20.9 ppm in accord with the expected chair conformation whereas the anti-diastereoisomer 23b gave corresponding signals at 28.1 and 24.6 ppm indicative of the expected twist-boat conformation.33

The reductive lithiation ³⁴ of the mixture of *O*, *S*-acetals **23a**, **b** using lithium di-*tert*-butylbiphenylide (LDBB) ^{35,36} in THF at -78 °C followed by quenching the reaction mixture with excess chlorotributylstannane gave the known ²⁶ 1,3-dioxan-4-yl-stannane **26** as a single diastereoisomer. The stereoconvergent formation of a single stannane from the mixture of *O*, *S*-acetals is a consequence of the radical anomeric effect ³⁷⁻³⁹ stabilising the conformation of the SOMO in **25**. Rapid donation of a second electron from the LDBB gave the axial organolithium, which is configurationally stable at low temperature, ^{28,29} and thence the axial stannane on transmetallation.

It was our original intention to use the 1,3-dioxan-4-ylcopper(I) reagent **30** (Scheme 7) as the nucleophilic partner in our synthesis of Cryptophycin 4. Rychnovsky had shown that the lithium reagent **27**, derived from transmetallation of the stannane **26** with BuLi, reacted with the terminal oxirane **28** in the presence of BF₃·OEt₂ to give the alkylation product **29** as a single diastereoisomer (62%) with clean retention of configuration.²⁶ However, a model study of the key alkylation reaction discovered an unexpected stereochemical problem. When the lithium reagent **27** was converted to its copper(I) derivative **30** at -78 °C and then added to a solution of the simple cationic η^3 -allylmolybdenum complex **31** in acetonitrile at -90 °C, the adducts **32a,b** were obtained as a mixture of separable diastereoisomers in 48% overall yield from **26**.

The formation of a significant proportion of the inversion product **32a** did not bode well for the Cryptophycin synthesis and it was the first example in our programme in which stereochemistry had been compromised in the addition of an α -heteroalkylcopper(I) nucleophile to a cationic η^3 -allylmolyb-



denum complex. We surmised that the origin of the problem lay in the repulsive 1,3-diaxial interaction between the Cu atom and the axial isopropylidene methyl group in 30. To test this hypothesis, the isopropylidene group was transacetalised in 89% yield to the separable benzylidene acetals 33a,b (a : b = 7 : 1) by treatment of 26 with benzaldehyde dimethylacetal in the presence of *p*-toluenesulfonic acid (Scheme 8). Equilibration of the minor diastereoisomer 33b under the same reaction conditions returned a mixture of 33a : 33b in the ratio 11 : 1. The stereochemistry of the diastereoisomers was deduced from ¹H NMR spectroscopic data summarised in Table 2. The major diastereoisomer 33a was identified by the strong NOE interactions between C2H and C4H whilst the minor diastereoisomer 33b displayed a strong NOE interaction between C2H and C6H in accord with the twist-boat conformation depicted.



Our suspicion that the configurational stability of the copper(I) reagent 30 was a consequence of steric destabilisation was lent some credence when the 1,3-dioxan-4-ylcopper(I) reagent 8 prepared from 33a was treated with cationic complex 31 (Scheme 8). The adduct 34 was obtained as a single diastereoisomer in 51% yield after oxidative decomplexation. However, in the next section we will show that reagent 8 does not preserve its stereochemical integrity in its reactions with cationic complexes.

Union of fragments 7 and 8 and completion of the synthesis

Stannane 33a was converted to the 1,3-dioxan-4-ylcopper(I) reagent 8 on an 8.5 mmol scale whilst carefully maintaining



the temperature at \leq -78 °C. A solution of the freshly prepared cationic complex 7 in acetonitrile, generated by adding nitrosonium tetrafluoroborate to the neutral complex 15 at 0 °C, was added in one portion to the copper reagent and after 1 h, aqueous workup was followed by oxidative decomplexation (O₂, CHCl₃). Column chromatography returned an inseparable mixture of regioisomeric olefins 6 and 35 in 71% yield whose relative proportion (1.2:1) was determined by integration of the alkene signals at 6.51 (d) and 6.26 (dd) ppm attributed to 6 and a multiplet at 5.64-5.50 attributed to 35 (Scheme 9). A further pair of inseparable regioisomeric olefins (ca. 1 : 1) were also obtained in < 5% yield which were tentatively assigned structures 36 and 37. Evidence for the stereochemistry in 36 derived from the signal for C4H with a large ${}^{3}J$ coupling (11 Hz) with the axial proton at C5, and strong NOE interactions between the protons at C2, C4 and C6 indicative of their axial relationship.



Hydrolysis of the triisopropylsilyl and benzylidene acetal protecting groups from the mixture of 6 and 35 gave triols 38 and 39 which could be separated, albeit with some difficulty, by column chromatography (Scheme 10). Sodium periodate oxidation of triol 38 revealed a β -hydroxy aldehyde which

underwent a Wadsworth–Horner–Emmons olefination using trimethylphosphonoacetate and tetramethylguanidine in THF at low temperature to give ester **5** in 83% overall yield from **38** as a single isomer.⁴⁰ Comparison of spectroscopic data for **5** with those reported by Moore and Tius⁴¹ together with the conversion of **5** to Cryptophycin 4 confirmed the structure and stereochemistry of the target.⁵



Scheme 10

The formation of the diastereoisomers 36 and 37 in the key addition step was a minor vexation compared with the lack of regioselectivity in the formation of 6 and 35. The contrast with the good steric discrimination between the methyl and isopropyl termini observed in complex $2^{1,2}$ suggests that the methyl and phenyl groups have similar steric requirements in complex 7 thereby allowing the electronic directing effect of the nitrosyl ligand to predominate.4,13 Tangential evidence for this argument was gleaned by following the ligand exchange reaction (15 to 7) by ¹H NMR spectroscopy in CD₃CN: two major *endo* isomers (the kinetic products)^{21,42} were observed in the ratio 1.2: 1, paralleling the observed ratio of olefin products following alkylation. Upon standing in CD₃CN solution for 24 h, the two endo isomers isomerised to a mixture of four compounds, presumably two pairs of exo and endo isomers, in the ratio 2.3 : 2 : 1 : 1.2, as estimated from the intensities of cyclopentadienyl singlets at 5.69, 6.11, 6.22, and 6.02 ppm respectively.

Conclusions

of (2E,5S,6R,7E)-6-methyl-8-phenylocta-The synthesis 2,7-dienoic acid (5) with the correct relative and absolute stereochemistry at C5 and C6 proved that (a) the key coupling step had occurred anti to the molybdenum in 7; (b) the nucleophile 8 added predominantly with retention of configuration; and (c) the oxidative addition of Mo(CO)₄(THF)₂ to allylic benzoates occurred with clean retention. The complete retention of stereochemistry in the addition of 1,3-dioxan-4-ylcopper(I) reagent 8 to the simple cationic complex 31 and the formation of epimeric adducts from the addition of 8 and 30 to cationic complexes 7 and 31 respectively shows that erosion in the stereochemical integrity of the nucleophile, though a rare event, may be influenced by the structure of the cationic complex, and by adverse steric interactions in the nucleophile. $Mo(CO)_4(THF)_2$ has been developed as an easily prepared and highly reactive reagent for the formation of η^3 -allylmolybdenum complexes from allylic benzoates, including trisubstituted systems which have hitherto been inaccessible by conventional reagents. Finally, we have established that 1,3dioxan-4-ylcopper(I) reagents are effective nucleophilic partners that form adducts rapidly and stereoselectively with cationic η^3 -allylmolybdenum complexes.⁴³

Experimental

Organic extracts were dried using magnesium sulfate (MgSO₄) unless otherwise specified, and were concentrated using a rotary evaporator. Diethyl ether and tetrahydrofuran were freshly distilled from sodium benzophenone ketyl under nitrogen prior to use. Eluants used in the purification of the Mo complexes were degassed by sparging with dry nitrogen for 20–30 minutes before use. CuBr·SMe₂ was prepared by the procedure of Taylor⁴⁴ and purified by recrystallisation before use. Commercial *n*-butyllithium was titrated against 1,3-diphenylacetone*p*-tosylhydrazone prior to use.⁴⁵

Specific optical rotations $([a]_D)$ were measured at ambient temperature (21±3 °C) on an Optical Activity polAAr 2000 polarimeter using a 5 mL cell with a 1 dm path length or a 0.5 mL cell with a 0.05 dm path length. Infra-red (IR) spectroscopic details are reported as v_{max} in cm⁻¹, followed by an intensity descriptor: s = strong, m = medium, br = broad; weak absorptions are not recorded. ¹H and ¹³C NMR spectra were recorded in CDCl₃, C₆D₆ or CD₃CN solution in 5 mm diameter tubes, and the chemical shift in ppm is quoted relative to the residual signals of chloroform ($\delta_{\rm H}$ 7.27, $\delta_{\rm C}$ 77.2), benzene ($\delta_{\rm H}$ 7.27, $\delta_{\rm C}$ 128.4) or acetonitrile ($\delta_{\rm H}$ 2.00, $\delta_{\rm C}$ 117.7) unless specified otherwise. Coupling constants (J) are reported in Hz. ¹H NMR signal assignments are based on COSY and HMQC correlations. ¹³C NMR signal assignments are based on DEPT and C-H correlation experiments. ⁹⁵Mo NMR (13 MHz) spectra were recorded on a Bruker WP200SY spectrometer and were referenced externally to $Na_2[MoO_4]$.^{46,47} Low and high resolution mass spectra were run on a JEOL MStation JMS-700 spectrometer. Ion mass/charge (m/z) ratios are reported as values in atomic mass units followed, in parenthesis, by the peak intensity relative to the base peak (100%). GCMS was performed on the above spectrometer, using a Chrompack WCOT Fused Silica column (25 m × 0.25 mm, CP-SIL 8CB-MS stationary phase), initial temperature and heating rates are specified for individual cases.

(2S,3E)-4-Phenylbut-3-en-2-ol (11) and (1R,2E)-acetic acid 1-methyl-3-phenylallyl ester (12)

A suspension of Novozyme 435 (66 mg), crushed activated 4 Å molecular sieves (330 mg), (RS)-11 (660 mg, 4.45 mmol) and vinyl acetate (10.3 mL, 111 mmol) in pentane (20 mL) was shaken gently at rt for 10 h. ¹H NMR spectroscopy of the crude reaction mixture indicated \geq 50% conversion. After filtration and concentration in vacuo, the residue was purified by column chromatography (SiO₂, ether : hexanes = $2: 8 \rightarrow 4: 6$) to give acetate (R)-12 (390 mg, 2.05 mmol, 46%) as a colourless oil, and alcohol (S)-11 (300 mg, 2.02 mmol, 45%) as a colourless oil which solidified upon standing. Alcohol (S)-11 gave mp 29–30 °C (hexanes–dichloromethane); lit.⁴⁸ mp 31–33 °C; $[a]_{\rm D} =$ -34.1 (c 2.34, CHCl₃); lit.⁴⁹ [a]_D (enantiomer) = +34.2 (c 1.77, CHCl₃). ¹H and ¹³C NMR spectroscopic data were in accordance with literature data.^{50,51} The enantiomeric ratio for alcohol 11 was estimated as 97 : 3 via formation of the corresponding (R)-acetoxyphenylacetic ester 13 by an analogous procedure to that detailed above.

Acetate (*R*)-**12** gave $[a]_{D} = +143.1$ (*c* 3.38, CHCl₃); lit.⁵² $[a]_{D} = +151.1$ (*c* 5.27, CHCl₃). ¹H NMR and IR spectroscopic data were in accordance with literature data.⁵³ ¹³C NMR (100 MHz, CDCl₃): $\delta = 170.5$ (COMe), 136.5 (C, Ph), 131.7 (CH, Ph), 129.0 (CH, Ph), 128.7 (2CH, Ph), 128.0 (CH, Ph), 126.7 (2CH, Ph), 71.1 (C1H), 21.5 (COMe), 20.5 (C1-Me). The enantiomeric ratio for acetate (*R*)-**12** was estimated as 96 : 4 by cleavage of the acetate (10 wt% K₂CO₃, MeOH, rt, 15 h) and formation of the corresponding (*R*)-acetoxyphenylacetic ester.

(*R*)-Acetoxyphenylacetic acid (1*S*)-1-methyl-3-phenylallyl ester [(*R*,*S*)-13]

To a solution of alcohol (*S*)-11 (41 mg, 0.28 mmol), (*R*)acetoxyphenylacetic acid (59 mg, 0.30 mmol) and DMAP (2 mg, 0.01 mmol) in CH₂Cl₂ (10 mL) at 0 °C under N₂ was added DCC (86 mg, 0.41 mmol). The mixture was stirred at 0 °C for 10 min and at rt for 50 min before filtering through Celite and washing with Et₂O. After drying, filtration and concentration *in vacuo*, the residue was purified by column chromatography (SiO₂, ether : hexanes = 3 : 7) to give the title compound (76 mg, 0.23 mmol, 84%) as a colourless oil. The diastereoisomeric ratio at C1 was estimated as 97 : 3 *via* integration of the C3H signals in the ¹H NMR spectrum: δ = 6.56 (d, *J* = 16.0, (1*S*)-diastereoisomer), δ = 6.26 (d, *J* = 16.0, (1*R*)diastereoisomer), with reference to a sample prepared from (*RS*)-11.

 $[a]_{\rm D} = -107.7 \ (c \ 2.32, \text{CHCl}_3).$

IR (film): $v = 1755 \text{ s cm}^{-1}$

¹H NMR (400 MHz, CDCl₃ referenced to added TMS): $\delta = 7.50-7.19$ (10H, m, Ph), 6.58 (1H, d, J = 16.0 Hz, PhCH), 6.16 (1H, dd, J = 16.0, 6.4 Hz, PhCH=CH), 5.95 (1H, s, CHOAc), 5.55 (1H, ddq, J = 6.4, 1.1, 6.5 Hz, CHCH₃), 2.17 (3H, s, OAc), 1.27 (3H, d, J = 6.5 Hz, CHCH₃).

¹³C NMR (100 MHz, CDCl₃): δ = 170.3 (C=O), 168.2 (C=O), 136.3 (C, Ph), 134.0 (C, Ph), 131.9 (CH), 129.2 (CH or Ph), 128.8 (2CH, Ph), 128.6 (2CH, Ph), 128.0 (2CH), 127.7 (2CH, Ph), 126.7 (2CH, Ph), 74.8 (CHOAc), 72.6 (CH), 20.8 (CH₃CO), 20.0 (CH₃CH).

LRMS (EI⁺ mode): *m*/*z* = 324.2 [M⁺⁺, 2%], 264.2 (7), 131.1 (100), 118.1 (40), 107.1 (32), 91.1 (20), 43.0 (17).

HRMS (EI⁺ mode): found M⁺⁺, 324.1359. $C_{20}H_{20}O_4$ requires M, 324.1362.

(*R*)-Acetoxyphenylacetic acid (1*R*)-1-methyl-3-phenylallyl ester [(*R*,*R*)-13]

 $[a]_{\rm D} = -2.6 \ (c \ 1.40, \ {\rm CHCl}_3).$

IR (film): v = 1763 s, 1743 s cm⁻¹.

¹H NMR (400 MHz, CDCl₃ referenced to added TMS): $\delta = 7.49-7.18$ (10H, Ph), 6.26 (1H, d, J = 16.0 Hz, PhCH), 5.98 (1H, dd, J = 16.0, 6.2 Hz, PhCH=CH), 5.95 (1H, s, CHOAc), 5.55 (1H, ddq, J = 6.4, 1.2, 6.2 Hz, CHCH₃), 2.19 (3H, s, OAc), 1.42 (3H, d, J = 6.4 Hz, CHCH₃).

¹³C NMR (100 MHz, CDCl₃): δ = 170.5 (C=O), 168.2 (C=O), 136.3 (C), 134.0 (C), 131.4 (CH), 129.4 (CH), 128.9 (2CH), 128.6 (3CH), 128.0 (3CH), 127.9 (CH), 126.6 (CH), 74.8 (CHOAc), 72.4 (CH–O), 20.9 (CH₃CO), 20.4 (CH₃CH).

LRMS (CI⁺ mode, NH₃): $m/z = 342.1 [(M + NH_4)^+, 14\%]$, 212.1 (14), 131.1 (100).

(1S,2E)-Benzoic acid 1-methyl-3-phenylallyl ester [(S)-14]

To a solution of alcohol (*S*)-**11** (3.82 g, 25.8 mmol) and 4-dimethylaminopyridine (10 mg) in CH₂Cl₂ (30 mL) at rt under N₂ was added benzoyl chloride (3.3 mL, 28.4 mmol) and triethylamine (4.0 mL, 28.4 mmol). The solution was stirred at rt for 18 h before the addition of HCl (2 M, 30 mL). The phases were separated and the aqueous phase extracted with CH₂Cl₂ (3 × 30 mL). The combined organic phases were washed with brine (50 mL), dried, filtered and concentrated *in vacuo*. The pale yellow solid residue was purified by recrystallisation from hexanes to give the title compound (5.89 g, 23.3 mmol, 90%) as a white solid: mp = 79–80 °C; $[a]_{\rm D}$ = +1.46 (*c* 7.56, CDCl₃); lit.⁴⁹ $[a]_{\rm D}$ = +0.42 (*c* 8.16 CHCl₃).

IR (KBr): $v = 1709 \text{ s cm}^{-1}$

¹H NMR (400 MHz, CDCl₃ referenced to added TMS): $\delta = 8.10-8.06$ (2H, m, Ph), 7.55–7.21 (8H, m, Ph), 6.69 (1H, d, J = 16.0 Hz, PhCH), 6.30 (1H, dd, J = 16.0, 6.6 Hz, PhCH= CH), 5.79 (1H, ddq, J = 6.5, 1.1, 6.5 Hz, CHCH₃), 1.54 (3H, d, J = 6.5 Hz, CHCH₃). ¹³C NMR (100 MHz, CDCl₃): δ = 165.9 (*C*OPh), 136.5 (C), 133.0 (CH), 131.8 (CH), 131.1 (CH), 129.7 (2CH), 129.0 (CH), 128.7 (2CH), 128.5 (2CH), 128.0 (CH), 126.7 (2CH), 71.7 (CH), 20.6 (CH₃).

syn-syn-Dicarbonyl(η^5 -cyclopentadienyl)-[(1,2,3- η)-(1*R*,2*S*,3*S*)-1-phenyl-2-but-2-en-1-yl]molybdenum (15)

Procedure A. To a solution of $Mo(CO)_6$ (512 mg, 1.94 mmol) in degassed THF (25 mL) under N₂ was added pyridine (0.31 mL, 3.88 mmol) and the solution brought to reflux. After refluxing for 12 h, a solution of benzoate (*S*)-14 (465 mg, 1.84 mmol) in degassed THF (1.5 mL) was added dropwise *via* syringe to the red-orange solution, which was refluxed for a further 18 h before cooling to rt over 1 h. Freshly prepared LiCp (7.1 mL of a 0.29 M solution in THF was added and the dark red-brown solution stirred at rt under N₂ for 1 h. The solution was transferred *via* syringe to a round-bottomed flask and concentrated *in vacuo* to a volume of approximately 10 mL, before purification by column chromatography (Al₂O₃, degassed hexanes–Et₂O, 2 : 1, under N₂) and concentration *in vacuo*. The title compound was obtained as a fine yellow crystalline solid (597 mg, 1.71 mmol, 88%).

Procedure B. A solution of $Mo(CO)_6$ (0.804 g, 3.04 mol) in degassed THF (25 mL) was heated to reflux under N₂ whereupon benzoate (S)-14 (0.732 g, 2.9 mmol) in degassed THF (2 mL) was added dropwise *via* syringe. After addition was complete the mixture was refluxed for a further 12 h. The mixture was allowed to cool to rt and a freshly prepared solution of LiCp (0.3 M, 10 mL) was added. After stirring at rt for 1 h, workup as described above gave the title complex (0.939 g, 2.9 mmol, 93%).

Neutral complex 15 was generally used without further purification, but for analytical purposes it could be purified by recrystallisation from pentane to give fine yellow needles: mp 85–88 °C; $[a]_{\rm D} = +8.0$ (*c* 0.67, CHCl₃).

IR (KBr): v = 1917 s, 1839 s cm⁻¹.

¹H NMR (400 MHz, CDCl₃ referenced to added TMS): $\delta = 7.30-7.19$ (3H, m, Ph), 7.12–7.08 (2H, m, Ph), 5.10 (5H, s, Cp), 4.88 (1H, t, J = 9.6 Hz, PhCH–CH–CH), 2.35 (1H, d, J = 10.0 Hz, PhCH–CH–CH), 1.86 (3H, d, J = 6.0 Hz, CHCH₃), 1.78–1.73 (1H, m, PhCH–CH–CH).

¹³C NMR (100 MHz, CDCl₃): δ = 239.7 (CO), 239.6 (CO), 142.1 (C, Ph), 128.6 (2CH, Ph), 125.9 (CH, Ph), 125.1 (2CH, Ph), 93.9 (5CH, Cp), 68.5 (PhCH–CH–CH), 58.8 (PhCH–CH– CH), 58.4 (PhCH–CH–CH), 21.2 (CH₃).

⁹⁵Mo NMR (13 MHz, THF): $\delta_{exo} = -1617$, $\delta_{endo} = -1412$. exo : endo = 13 : 1.

LRMS (EI mode): m/z = 350.2 [(M(⁹⁸Mo))⁺⁺, 25%], 322.2 [(M(⁹⁸Mo)-CO)⁺⁺, 20], 292.2 (100).

Found: C, 58.60; H, 4.69. $C_{17}H_{16}O_2Mo$ requires C, 58.63; H, 4.63%.

syn-syn-Carbonyl-(nitrosyl)-(η^5 -cyclopentadienyl)-[(1,2,3- η)-(1R,2S,3S)-1-phenyl-2-but-2-en-1-yl]molybdenum tetrafluoroborate (7)

Cationic complex **15** was routinely prepared in a minimum volume (*ca.* 2–3 mL mmol⁻¹) of freshly distilled MeCN at 0 °C under N₂ by the addition of NOBF₄ (1.1 eq.) and transferred directly *via* cannula to a solution of the nucleophile. However, for characterisation purposes the title compound was prepared on a 3.4 mmol scale and transferred to Et₂O (200 mL) at 0 °C under N₂ to yield a light-brown solid after cooling to -60 °C for 15 min. Cationic complex 7 (518 mg, 1.20 mmol, 36%) was isolated by filtration under an atmosphere of N₂: IR (solution in CD₃CN): v = 2080 s, 1720 s cm⁻¹. Complex 7 was initially isolated as a mixture of two major isomers (presumably a pair of *endo* isomers), in the approximate ratio 1.2 : 1. On standing at rt for 24 h, a mixture of four isomers was obtained in a ratio

of approximately 2.3 : 2 : 1 : 1.2, as estimated by the integrations of Cp singlets at 5.69, 6.11, 6.22 and 6.02 ppm respectively.

¹H NMR (360 MHz, CD₃CN) data for the initial (endo) isomers: $\delta = 7.54-7.35$ (10H, m, Ph), 6.11 (5H, s, Cp), 5.69 (5H, s, Cp), 6.23–5.93 (2H, m, PhCH–CH–CH), 5.28 (1H, d, J=11.7 Hz, PhCH-CH-CH), 5.20 (1H, d, J = 13.4 Hz, PhCH-CH-CH), 3.95 (1H, dq, J = 12.9, 6.2 Hz, PhCH–CH–CH), 3.76 (1H, dq, J = 12.3, 6.2 Hz, PhCH–CH–CH), 2.47 (3H, d, J = 5.9 Hz, CHCH₃), 2.30 (3H, d, J = 6.3 Hz, CHCH₃); partial data for the *exo*-isomers: $\delta = 6.22$ (5H, s, Cp), 6.02 (5H, s, Cp), 4.77 (1H, d, J = 13.8 Hz, PhCH-CH-CH), 4.51-4.44 (2H, m, PhCH-CH-CH), 4.40 (1H, d, J = 13.0 Hz, PhCH–CH–CH), 2.42 (3H, d, J = 6.4 Hz, CHCH₃). Signals for C2H and the second C4H doublet obscured by major isomer peaks at 6.23-5.93 ppm and 2.30 ppm respectively.

¹³C NMR (100 MHz, CD₃CN, equilibrium mixture of four isomers): $\delta = 214.9$ (C), 213.9 (C), 211.0 (C), 209.5 (C), 136.8 (C), 135.8 (C), 135.4 (C), 134.0 (C), 131.4 (2CH), 130.7 (2CH), 130.0 (2CH), 129.8 (2CH), 129.7 (2CH), 129.5 (2CH), 129.4 (2CH), 128.0 (2CH), 127.7 (2CH), 127.6 (2CH), 106.7 (CH), 106.5 (CH), 104.2 (CH), 103.3 (5CH), 102.5 (5CH), 102.4 (5CH), 101.8 (5CH), 101.0 (CH), 94.6 (CH), 93.4 (CH), 92.3 (CH), 88.0 (CH), 83.3 (CH), 80.6 (CH), 76.8 (CH), 74.6 (CH), 21.1 (CH₃), 19.6 (CH₃), 18.9 (CH₃), 18.2 (CH₃).

⁹⁵Mo NMR (13 MHz, MeCN): $\delta = -1293, -1339, -1383$ ppm, in the approximate ratio 1:2.5:4, with approximate line widths of 210 Hz, 206 Hz, 290 Hz respectively.

HRMS (FAB mode, nitrobenzyl alcohol matrix): found M⁺ 352.0235. C₁₆H₁₆O₂N⁹⁸Mo requires M, 352.0238. Found M⁺⁺, 350.0246. C₁₆H₁₆O₂N⁹⁶Mo requires M, 350.0235.

Benzoic acid 1,2-dimethyl-2-butenyl ester (16e)

To a solution of 1,2-dimethyl-2-butenol (1.46 g, 14.6 mmol) in CH₂Cl₂ (60 mL) at 0 °C was added DMAP (0.1 g, 0.73 mmol), NEt₃ (3.1 mL, 21.9 mmol) and benzoyl chloride (1.9 mL, 16 mmol). The cooling bath was removed and the reaction mixture allowed to stir at ambient temperature for 12 h whereupon the excess benzoyl chloride was destroyed by the addition of 3-dimethylaminopropylamine (1 mL). The reaction mixture was washed with HCl (1 M, 2 × 45 mL) and NaHCO₃ (1 M, 2×45 mL). The organic layer was dried (MgSO₄) and concentrated in vacuo. The residue was purified by column chromatography (SiO₂, Et_2O : hexanes = 1 : 4) to give the title compound (1.82 g, 8.9 mmol, 61%) as a colourless oil.

IR (film): $v = 1720 \text{ s cm}^{-1}$

¹H NMR (300 MHz, CDCl₃): *δ* = 8.04–8.08 (2H, m, *o*-ArH), 7.53-7.58 (1H, m, p-ArH), 7.41-7.47 (2H, m, m-ArH), 5.64 (1H, qq, J = 6.7, 0.3 Hz, C3H), 5.52 (1H, q, J = 6.5 Hz, C1H), 1.72 (3H, s, C2CH₃), 1.63 (3H, d, J = 6.5 Hz, C4H₃), 1.43 (3H, d, J = 6.5 Hz, C1CH₃).

¹³C NMR (75 MHz, CDCl₃): δ = 166.2 (CO), 135.5 (C2), 133.1 (CH), 131.3 (C), 129.7 (2CH), 128.7 (2CH), 122.1 (C3H), 76.1 (C1H), 19.6 (C1CH₃), 13.5 (C2CH₃), 12.1 (C4H₃),

Found: C, 76.41; H, 7.88. C₁₃H₁₆O₂ requires C, 76.44; H, 7.90%.

(4S,2E)-2-Methyl-4-(benzoyloxy)-pent-2-enoic acid ethyl ester (16h)

Benzoate 16h, prepared from (4S,2E)-ethyl-4-hydroxy-2-methylpent-2-enoate^{54,55} (0.18 g, 1.2 mmol) in 84% yield by the procedure described for 16e, was isolated as a colourless oil after purification by column chromatography (SiO₂, hexanes : $Et_2O = 10:1$).

 $[a]_{\rm D} = 74.9 \ (c \ 0.91, \ {\rm CHCl}_3).$

IR (film): v = 1717 s, 1659 m cm⁻¹.

¹H NMR (300 MHz, CDCl₃): δ = 7.98 (2H, dd, J = 8.5, 1.3 Hz, o-ArH), 7.48 (1H, td, J = 7.2, 1.2 Hz, p-ArH), 7.35 (2H, t, J = 7.2 Hz, *m*-ArH), 6.66 (1H, dd, J = 8.6 Hz, 1.4 Hz, C3H), 5.82 (1H, dq, J = 8.2, 6.7 Hz, C4H), 4.14 (2H, q, J = 7.2 Hz, OCH₂CH₃), 1.91 (3H, d, J = 1.1 Hz, C2CH₃), 1.4 (3H, d, J = 6.4 Hz, C5H₃), 1.23 (3H, t, J = 7.2 Hz, OCH₂CH₃).

¹³C NMR (75 MHz, CDCl₃): δ = 168.1 (C), 166.2 (C), 139.9 (CH), 133.5 (CH), 130.6 (C), 130.1 (CH), 130.0 (2CH), 128.8 (2CH), 68.7 (CH), 61.3 (CH₂), 20.2 (CH₃), 14.6 (CH₃), 13.3 (CH_{2})

LRMS (FAB mode): m/z = 263 [(M⁺ + H), 12%], 141 (100), 105 (51), 77 (7).

HRMS (ES mode): Found $(M^+ + H)$, 263.1280. $C_{15}H_{18}O_4 +$ H) requires M, 263.1283.

Dicarbonyl(n⁵-cyclopentadienyl)-(n³-propenyl)-molybdenum (17a)

Complex 17a, prepared from benzoate 16a^{56,57} in 86% yield by procedure A (10.8 mmol scale) and 86% yield by procedure B (5.5 mmol scale), was obtained as yellow needles: mp 136-139 °C (Et₂O-pentane); lit.⁵⁸ mp 135-138 °C (Et₂O-heptane). ¹H NMR spectroscopy indicated that 17a was a mixture of exo and endo isomers (3.3:1) in good agreement with literature data.^{21,58} ⁹⁵Mo NMR (13 MHz, THF): $\delta_{exo} = -1856$, $\delta_{endo} =$ $-1648.^{21}$

Dicarbonyl(n⁵-cyclopentadienyl)-(n³-2-methylallyl)-molybdenum (17b)

Complex 17b, prepared from benzoate 16b⁵⁹ in 82% yield by procedure A (3.3 mmol scale) and 85% yield by procedure B (4.6 mmol scale), was obtained as a yellow solid: mp 76-78 °C (Et₂O-pentane); lit.⁶⁰ mp 79-81 °C. The IR, ¹H NMR and ⁹⁵Mo NMR spectroscopic data agreed with those reported by Faller and co-workers.21,60

¹³C NMR (75 MHz, CDCl₃): δ = 105.4 (C), 90.5 (5CH, Cp), 38.6 (2CH₂), 23.6 (CH₃).

Dicarbonyl-(η^5 -cyclopentadienyl)-(2,3,4- η -2-methyl-3-butenyl)molybdenum (17c)

Complex 17c, prepared from benzoate 16c⁶¹ in 58% yield by procedure A (2.1 mmol scale) and 65% yield by procedure B (3.2 mmol scale), was obtained as a yellow solid: mp 61–63 °C (Et₂O-pentane); lit.⁶⁰ mp 65-69 °C (Et₂O-hexane). The IR, ¹H NMR and ⁹⁵Mo NMR spectroscopic data agreed with those reported by Faller and co-workers.21,60

¹³C NMR (75 MHz, CDCl₃): δ = 92.2 (5CH, Cp), 81.5 (C2), 68.6 (C3H), 31.1 (C4H₂), 30.8 (CH₃), 14.4 (CH₃).

syn, syn-Dicarbonyl-(η^5 -cyclopentadienyl)-[2,3,4- η -(2R,3S,4S)-1-ethoxy-1-oxopent-2-enyl]molybdenum (17d)

Complex 17d, prepared from benzoate 16d in 70% yield by procedure A (3.2 mmol scale) and 82% yield by procedure B (0.3 mmol scale), was obtained as an air-sensitive viscous yellow-orange oil. The ¹H and ¹³C NMR spectroscopic data agreed with those reported.62

Dicarbonyl-(n⁵-cyclopentadienyl)-(2,3,4-n-3-methyl-3-pentenyl)molvbdenum (17e)

The title complex 17e, prepared from benzoate 16e in 80% yield by procedure A (1.7 mmol scale) and 85% yield by procedure B (3.7 mmol scale), was obtained as a yellow solid: mp 136-137 °C (Et₂O-pentane).

IR (film): v = 1930 s, 1850 s cm⁻¹.

¹H NMR (300 MHz, CDCl₃): δ = 4.75 (5H, s, CpH), 2.21 (2H, q, J = 6.0 Hz, C2H and C4H), 2.02 (6H, d, J = 6.0 Hz,C1H₃ and C5H₃), 1.82 (3H, s, C3H₃).

¹³C NMR (75 MHz, CDCl₃): δ = 105.7 (C3), 91.0 (5CH, Cp), 51.8 (C2H and C4H), 16.8 (2CH₃), 13.3 (CH₃).

⁹⁵Mo NMR (13 MHz, CDCl₃): $\delta = -1487$.

HRMS (EI⁺ mode): found M⁺, 300.2010. C₁₂H₁₄O₂Mo requires M, 300.2088.

$Dicarbonyl-(\eta^{5}-cyclopentadienyl)-(2,3,4-\eta-2-methyl-3-pentenyl)-molybdenum (17f)$

Complex 17f, prepared from benzoate $16f^{63}$ in 50% yield by procedure A (1.4 mmol scale) and 58% yield by procedure B (1.7 mmol scale), was obtained as a dark yellow oil.

IR (film): v = 1931 s, 1848 s cm⁻

¹H NMR (300 MHz, CDCl₃): δ = 5.26 (5H, s, CpH), 4.05 (1H, d, *J* = 9.8 Hz, C3H), 1.93 (1H, m, C4H), 1.78 (3H, d, *J* = 6.3 Hz, C5H₃), 1.74 (3H, s, C1H₃), 0.99 (3H, s, CH₃).

¹³C NMR (75 MHz, CDCl₃): δ = 93.4 (5CH, Cp), 72.5 (C3H), 72.3 (C2), 55.7 (C4H), 31.2 (C2-*Me*), 23.1 (C1H₃), 21.6 (C5H₃). The sample deteriorated before the weak and broad carbonyl signals could be recorded.

⁹⁵Mo NMR (13 MHz, CDCl₃): $\delta = -1654$.

HRMS (EI⁺ mode): found M^{+*} , 300.2010. $C_{12}H_{14}O_2Mo$ requires M, 300.2088.

Dicarbonyl-(η^{5} -(cyclopentadienyl)-(1,2,3- η -2,4-dimethyl-2-pentenyl)-molybdenum (17g)

Complex 17g, prepared from benzoate $16g^{64}$ in 95% yield (2.15 mmol scale) by procedure B, was obtained as a yellow oil. IR (film): v = 1941 s, 1866 s cm⁻¹.

¹H NMR (300 MHz, C₆D₆): δ = 4.58 (5H, s, CpH), 2.55 (1H, s, C1H_{trans}), 2.40–2.25 (1H, m, C4H), 2.11 (1H, d, *J* = 9.7 Hz, C3H), 1.67 (3H, s, C2Me), 1.27 (1H, s, C1H_{cis}), 1.06–1.01 (6H, m, C4Me₂).

¹³C NMR (75 MHz, C_6D_6): $\delta = 242.8$ (CO), 242.3 (CO), 103.2 (C2), 91.1 (5CH, Cp), 71.4 (C3H), 36.6 (C1H₂), 30.2 (C4H), 25.9 (CH₃), 25.2 (CH₃), 19.3 (CH₃).

Satisfactory HRMS (electrospray) or microanalytical data could not be obtained for 17g.

Dicarbonyl-(η⁵-cyclopentadienyl)-(2,3,4-η-2-methyl-1-ethoxy-1oxopent-2-enyl)molybdenum (17h)

Complex **17g**, prepared from benzoate **16g** in 88% yield (0.76 mmol scale) by procedure B, was obtained as a yellow-orange oil:

 $[a]_{\rm D} = +41.3 \ (c \ 0.21, \ {\rm CHCl}_3).$

IR (film): v = 1949 s, 1868 s, 1693 s cm⁻¹.

¹H NMR (300 MHz, CDCl₃): $\delta = 4.97$ (1H, d, J = 10.7 Hz, C3H), 4.73 (5H, s, CpH), 4.07 (1H, dq, J = 10.75, 7.2 Hz, CH_AH_BCH₃), 3.96 (1H, dq, J = 10.75, 7.2 Hz, CH_AH_BCH₃), 2.34 (1H, dq, J = 10.7, 6.3 Hz, C4H), 1.51 (3H, d, J = 6.3 Hz, C5H₃), 1.18 (3H, s, C2CH₃), 1.02 (3H, t, J = 7.1 Hz, OCH₂CH₃).

¹³C NMR (300 MHz, CDCl₃): δ = 238.1 (CO), 237.7 (CO), 173.5 (CO), 93.2 (5CH, Cp), 73.4 (C4H), 62.9 (C2), 59.6 (C3H), 58.9 (CH₂), 19.5 (C2CH₃), 15.9 (C5H₃), 13.8 (CH₃).

LRMS (EI mode): $m/z = 360.2 \text{ (M}^{+*}, 8\%)$, 332.2 (M - CO, 20), 304.2 (M - 2CO, 37), 228.1 (100)

(3S)-3,4-Dihydroxybutyric acid methyl ester (18)

Diol 18, prepared in 89% yield on an 89 mmol scale by the method of Moriwake and co-workers, gave $[a]_{\rm D} = -23.2$ (*c* 1.22, CHCl₃); lit. $[a]_{\rm D} = -24.6$ (*c* 1.00, CHCl₃).^{30,65} ¹H and ¹³C NMR spectroscopic data were in accordance with literature data.⁶⁵

(3*S*)-3-Hydroxy-4-(triisopropylsilyloxy)butyric acid methyl ester (19)

To a solution of diol **18** (12.0 g, 89.3 mmol) and imidazole (12.2 g, 178.6 mmol) in *N*,*N*-dimethylformamide (100 mL) at 0 °C under N₂ was added triisopropylsilyl chloride (20.1 mL, 93.8 mmol). The solution was stirred at rt for 30 h and then poured into hexanes (250 mL) and H₂O (75 mL). The phases were separated and the organic phase washed with H₂O (2 × 50 mL), dried, filtered and concentrated *in vacuo*. The residue

was purified by column chromatography (SiO₂, ethyl acetate : hexanes = 1 : 9) to give the title compound (18.5 g, 63.6 mmol, 71%) as a colourless oil.

 $[a]_{\rm D} = -7.2 \ (c \ 1.06, \ {\rm CHCl}_3).$

IR (film): v = 3481 br m, 2944 s, 2867 s, 1736 s cm⁻¹.

¹H NMR (400 MHz, CDCl₃): $\delta = 4.11$ (1H, ddq, J = 7.6, 5.8, 4.8 Hz, C3H), 3.72 (1H, dd, J = 9.8, 4.9 Hz, C4 H_AH_B), 3.71 (3H, s, CO₂Me), 2.91 (1H, d, J = 4.8 Hz, OH), 3.66 (1H, dd, J = 9.8, 5.8 Hz, C4 H_AH_B), 2.58 (1H, dd, J = 16.0, 4.8 Hz, C2 H_AH_B), 2.52 (1H, dd, J = 16.0, 7.6 Hz, C2 H_AH_B), 1.06 (18H, d, J = 5.6 Hz, SiCH Me_2), 1.15–1.04 (3H, m, SiCHMe₂).

¹³C NMR (100 MHz, CDCl₃): $\delta = 172.7$ (C1), 68.8 (C3H), 66.6 (C4H₂), 51.9 (CO₂*Me*), 38.0 (C2H₂), 18.1 (6CH₃, SiCH*Me*₂), 12.0 (3CH, Si*C*HMe₂).

LRMS (CI mode, isobutane): $m/z = 291.2 [(M + H)^+, 100\%],$ 247.1 (15).

Found: C, 57.81; H, 10.37. $C_{14}H_{30}O_4Si$ requires: C, 57.89; H, 10.41%.

(3S)-3-Hydroxy-4-(triisopropylsilyloxy)butyric acid (20)

To a solution of ester **19** (38.6 g, 133 mmol) in MeOH (600 mL) was added 10% aqueous potassium carbonate solution (270 mL) and the mixture refluxed for 1.5 h. After cooling to rt, the mixture was acidified to pH 2 with 2 M HCl. After extraction with Et₂O (2 × 250 mL) and washing with brine (200 mL), the organic phase was dried, filtered, and concentrated *in vacuo*. The residue was purified by column chromatography (SiO₂, ethyl acetate : hexanes = 2 : 8 \rightarrow 1 : 1) to give the title compound (27.1 g, 98 mmol, 74%) as a colourless oil.

 $[a]_{\rm D} = -7.2 \ (c \ 0.83, \ {\rm CHCl}_3).$

IR (film): v = 3460 br, 1713 s cm⁻¹.

¹H NMR (400 MHz, CDCl₃): $\delta = 6.50$ (1H, br s, OH), 4.17–4.07 (1H, m, C3H), 3.73 (1H, dd, J = 9.8, 4.9 Hz, C4 H_AH_B), 3.68 (1H, dd, J = 9.8, 5.7 Hz, C4 H_AH_B), 2.63 (1H, dd, J = 16.2, 4.6 Hz, C2 H_AH_B), 2.56 (1H, dd, J = 16.2, 7.9 Hz, C2 H_AH_B), 1.05 (18H, d, J = 5.7 Hz, SiCH Me_2), 1.15–1.05 (3H, m, SiCHMe₂).

¹³C NMR (100 MHz, CDCl₃): δ = 177.6 (C1), 68.7 (C3H), 66.4 (C4H₂), 38.1 (C2H₂), 18.0 (6CH₃, SiCH*Me*₂), 12.0 (3CH, SiCHMe₂).

LRMS (CI mode, isobutane): $m/z = 277 [(M + H)^+, 100\%],$ 259 (14), 233 (23), 173 (19).

Found: C, 56.22; H, 10.03. C₁₃H₂₈O₄Si requires: C, 56.48; H, 10.21%.

(6*S*)-6-[(Triisopropylsilyloxy)methyl]-2,2-dimethyl-1,3-dioxan-4-one (21)

To a solution of acid **20** (7.45 g, 27.0 mmol) and 2-methoxypropene (3.10 mL, 32.3 mmol) in CH₂Cl₂ (250 mL) at rt under N₂ was added pyridinium *p*-toluenesulfonate (339 mg, 1.35 mmol). The clear solution was stirred at rt for 3 h before concentration *in vacuo*. The residue was purified by column chromatography (SiO₂, ether : hexanes = 4 : 6) to give the title compound (7.15 g, 22.6 mmol, 84%) as a clear oil: $[a]_D = -38.4$ (*c* 1.10, CHCl₃). Further elution yielded acid **20** (730 mg, 2.64 mmol, 10%).

IR (film): v = 2945 s, 2864 s, 1746 s cm⁻¹.

¹H NMR (400 MHz, CDCl₃): δ = 4.20 (1H, tt, *J* = 7.1, 4.8 Hz, C6H), 3.81 (1H, dd, *J* = 10.4, 4.8 Hz, CH_AH_BOTIPS), 3.74 (1H, dd, *J* = 10.4, 4.8 Hz, CH_AH_BOTIPS), 2.59 (2H, apparent d, *J* = 7.1 Hz, C5H₂), 1.59 and 1.57 (3H each, s, CMe₂), 1.05 (18H, d, *J* = 5.2 Hz, SiCHMe₂), 1.14–1.03 (3H, m, SiCHMe₂).

¹³C NMR (100 MHz, CDCl₃): δ = 168.1 (C4), 106.1 (C2), 68.7 (C6H), 65.6 (CH₂OTIPS), 31.8 (C5H₂), 29.1 (CH₃), 25.0 (CH₃), 18.0 (6CH₃, SiCH*Me*₂), 12.0 (3CH, SiCHMe₂).

LRMS (CI mode, isobutane): m/z = 317.3 [(M + H)⁺, 100%], 259.2 (16).

Found: C, 60.71; H, 10.07. C₁₆H₃₂O₄Si requires: C, 60.72; H, 10.19%.

(4*S*,6*S*)-4-Acetoxy-2,2-dimethyl-6-(triisopropylsilyloxymethyl)-1,3-dioxane (22)

To a solution of dioxanone 21 (19.1 g, 60.4 mmol) in CH₂Cl₂ (180 mL) at -78 °C under N₂ was added neat DIBAL-H (11.3 mL, 63.4 mmol) dropwise. After stirring -78 °C for 1 h, pyridine (14.6 mL, 181 mmol), 4-dimethylaminopyridine (8.11 g, 66.4 mmol) in CH₂Cl₂ (50 mL) and acetic anhydride (22.8 mL, 241 mmol) were added and the clear solution stirred at -78 °C for a further 1.5 h before the addition of aqueous NH₄Cl (100 mL) and aqueous sodium potassium tartrate (100 mL). The solution was allowed to warm to rt with vigorous stirring over 1 h. The phases were separated, and the aqueous phase extracted with CH_2Cl_2 (3 × 100 mL). The combined organic phases were washed with ice-cold 1 M NaHSO₄ (3 \times 100 mL), aqueous NaHCO₂ (2×100 mL) and brine (100 mL), dried, filtered and concentrated in vacuo to yield the crude product as a colourless oil. The residue was purified by column chromatography (SiO₂, ether : hexanes = 1 : 9) to give the title compound (18.3 g, 50.7 mmol, 84%) as a clear oil. ¹³C NMR spectroscopy indicated that acetate 22 was a single diastereoisomer, identified as the svn-1,3-diol acetonide isomer by reference to the shifts of the acetonide methyl signals, and to the coupling constants of C4H.66,67

 $[a]_{\rm D} = -5.1$ (c 1.26, CHCl₃).

IR (film): $v = 1757 \text{ s cm}^{-1}$.

¹H NMR (400 MHz, CDCl₃): $\delta = 6.18$ (1H, dd J = 10.0, 3.0 Hz, C4H), 4.01 (1H, dddd, J = 11.7, 6.3, 4.8, 2.5 Hz, C6H), 3.81 (1H, dd, J = 9.8, 5.0 Hz, CH_AH_BOTIPS), 3.61 (1H, dd, J = 9.6, 6.4 Hz, CH_AH_BOTIPS), 2.11 (3H, s, COMe), 1.96 (1H, dt, J = 12.4, 2.8 Hz, $C5H_AH_B$), 1.56–1.43 (1H, m, $C5H_AH_B$), 1.52 and 1.44 (3H each, s, CMe₂), 1.13–1.01 (3H, m, $SiCHMe_2$), 1.05 (18H, d, J = 4.8 Hz, $SiCHMe_2$).

¹³C NMR (100 MHz, CDCl₃): δ = 169.6 (COMe), 100.7 (C2), 89.6 (C4H), 69.5 (CH₂OTIPS), 66.8 (C6H), 33.1 (C5H₂), 29.8 (3, CMe₂), 21.4 (3, COMe), 20.9 (3, CMe₂), 18.1 (6CH₃, SiCHMe₂), 12.1 (3CH, SiCHMe₂).

LRMS (CI mode, NH₃): $m/z = 378.3 [(M + NH_4)^+, 67\%]$, 318.3 (100), 301.2 (92).

Found: C, 59.95; H, 9.88. C₁₈H₃₆O₅Si requires: C, 59.96; H, 10.06%.

(4*R*,6*S*)-2,2-Dimethyl-4-phenylsulfanyl-6-(triisopropylsilyloxymethyl)-1,3-dioxane (23b) and (4*S*,6*S*)-2,2-dimethyl-4-phenylsulfanyl-6-(triisopropylsilyloxymethyl)-1,3-dioxane (23a)

To a solution of acetate 22 (9.90 g, 27.5 mmol) in CH₂Cl₂ (110 mL) at -70 °C under N₂ was added phenylthiotrimethylsilane (5.5 mL, 28.8 mmol) and ZnCl₂ (0.82 mL of a 1.0 M solution in ether, 0.82 mmol) dropwise. The light brown solution was stirred at -70 °C for 17 h before addition of 1 M NaOH (50 mL) and warming to rt. The phases were separated, and the aqueous phase extracted with CH_2Cl_2 (3 × 50 mL). The combined organic phases were washed with 1 M NaOH (50 mL) and brine (50 mL), dried, filtered and concentrated in vacuo. The residue was purified by column chromatography $(SiO_2, ether : hexanes = 2 : 98 \rightarrow 4 : 96)$ to give a mixture of the title compounds (9.74 g, 23.7 mmol, 86%) as a clear oil. ¹H and ¹³C NMR spectroscopy indicated a ratio of 23b : 23a of approximately 7 : 3.66,67 For analytical purposes, a sample of isomers 23b and 23a was separated by careful column chromatography.

Alternative procedure: ZnCl₂ (1.9 mL of a 1.0 M solution in ether, 1.9 mmol) was added dropwise to a solution of acetate **22** (17.4 g, 48.4 mmol) and thiophenol (5.2 mL, 50.8 mmol) in CH₂Cl₂ (240 mL) at -30 °C under N₂. After stirring for 15 min at -30 °C NaOH (1 M, 100 mL) was added and the mixture allowed to warm to rt. Workup and purification as above yielded a mixture of the title compounds (17.3 g, 42.1 mmol) as a colourless oil. ¹H and ¹³C NMR spectroscopy indicated a ratio of **23b** : **23a** of approximately 1 : 9.^{66,67}

Spectroscopic data for thioether **23b**: $(R_f = 0.85, Et_2O : PhMe = 2:98)$

 $[a]_{\rm D} = +85.0 \ (c \ 0.22, \ {\rm CHCl}_3).$

IR (film): v = 2942 s, 2859 s, 1461 m, 1382 m, 1137 m, 1114 m, 873 m, 688 m cm⁻¹.

¹H NMR (360 MHz, CDCl₃): δ = 7.52–7.47 (2H, m, Ph), 7.33–7.22 (3H, m, Ph), 5.50 (1H, t, *J* = 5.8 Hz, C4H), 4.17 (1H, ddt, *J* = 10.2, 4.7, 5.5 Hz, C6H), 3.80 (1H, dd, *J* = 10.2, 5.5 Hz, CH_AH_BOTIPS), 3.64 (1H, dd, *J* = 10.2, 5.7 Hz, CH_AH_BOTIPS), 2.08 (1H, ddd, *J* = 13.5, 10.1, 6.0 Hz, C5H_AH_B), 1.99 (1H, ddd, *J* = 13.5, 5.7, 4.7 Hz, C5H_AH_B), 1.61 and 1.38 (3H each, s, CMe₂), 1.14–1.04 (3H, m, SiCHMe₂), 1.07 (18H, d, *J* = 4.5 Hz, SiCHMe₂).

¹³C NMR (90 MHz, CDCl₃): δ = 135.6 (C, Ph), 131.0 (2CH, Ph), 129.0 (2CH, Ph), 127.1 (CH, Ph), 101.1 (C2), 78.6 (C4H or C6H), 67.8 (C4H or C6H), 66.5 (CH₂OTIPS), 34.0 (C5H₂), 28.1 (CMe₂), 24.6 (CMe₂), 18.1 (6CH₃, SiCHMe₂), 12.1 (3CH, SiCHMe₂).

LRMS (FAB⁺ mode): m/z = 433.4 [(M + Na)⁺, 22%], 335.4 (14), 301.4 (47), 243.3 (82), 173.2 (100), 157.2 (73), 115.3 (43).

HRMS (FAB⁺ mode, PEG): found $[M + Na]^+$, 433.2210. C₂₂H₃₈O₃SSiNa requires 433.2209.

Compound **23a** ($R_f = 0.78$, Et₂O : PhMe = 2:98) has been described previously, with only the following ¹³C NMR data reported: $\delta = 30.0$ (Me), 19.9 (Me) ppm.⁶⁶

 $[a]_{\rm D} = -54.2 \ (c \ 0.36, \text{CHCl}_3).$

IR (film): v = 2938 s, 2859 s, 1138 m, 1117 m, 955 m, 881 m, 689 m cm⁻¹.

¹H NMR (400 MHz, CDCl₃): δ = 7.50–7.48 (2H, m, Ph), 7.32–7.23 (3H, m, Ph), 5.31 (1H, dd, *J* = 12.0, 2.5 Hz, C4H), 4.02 (1H, dddd, *J* = 11.3, 6.4, 4.9, 2.4 Hz, C6H), 3.76 (1H, dd, *J* = 9.8, 4.9 Hz, CH_AH_BOTIPS), 3.54 (1H, dd, *J* = 9.8, 6.4 Hz, CH_AH_BOTIPS), 1.98 (1H, dt, *J* = 12.9, 12.5 Hz, C5H_AH_B), 1.61–1.52 (1H, m, C5H_AH_B), 1.55 and 1.52 (3H each, s, CMe₂), 1.12–1.04 (3H, m, SiCHMe₂), 1.04 (18H, d, *J* = 4.5 Hz, SiCHMe₂).

¹³C NMR (100 MHz, CDCl₃): δ = 134.3 (C, Ph), 131.4 (2CH, 1, Ph), 129.0 (2CH, 1, Ph), 127.3 (CH, Ph), 100.3 (C2), 77.7 (C4H or C6H), 70.5 (C4H or C6H), 66.9 (CH₂OTIPS), 34.0 (C5H₂), 30.1 (CMe₂), 20.0 (CMe₂), 18.1 (6CH₃, SiCH*Me*₂), 12.1 (3CH, SiCHMe₂).

LRMS (CI mode, NH₃): m/z = 428.2 [(M + NH₄)⁺, 34%], 370.2 (39), 318.2 (69), 301.2 (100), 283.2 (81), 260.2 (31), 151.1 (39).

HRMS (CI⁺ mode, isobutane): found $[M + H]^+$, 411.2389. C₂₂H₃₉O₃SSi requires 411.2389.

Found (mixture of isomers): C, 64.36; H, 9.41. C₂₂H₃₈O₃SSi requires: C, 64.34; H, 9.33%.

4,4-Bis-phenylsulfanyl-1-(triisopropylsilyloxy)butan-2-ol (24)

The title compound was obtained in an initial attempt to synthesise thioethers **23b** and **23a** by the following procedure: a solution of acetate **22** (57 mg, 0.16 mmol) and thiophenol (0.03 mL, 0.32 mmol) in CH₂Cl₂ (5 mL) was cooled to $-78 \,^{\circ}$ C under N₂ and BF₃·OEt₂ (0.02 mL, 0.19 mmol) was added dropwise. After stirring at $-78 \,^{\circ}$ C for 1 h, NaOH (1 M, 2 mL) was added, the mixture was warmed to rt and the phases were separated. The aqueous phase was extracted with CH₂Cl₂ (3 × 10 mL), and the combined organic phases washed with NaOH (1 M, 2 × 10 mL), brine (10 mL), dried, filtered and concentrated *in vacuo*. The residue was purified by column chromatography (SiO₂, Et₂O : hexanes = 1 : 9) to give the title compound (55 mg, 0.12 mmol, 75%) as a colourless oil.

 $[a]_{\rm D} = -8.1 \ (c \ 0.42, \ {\rm CHCl}_3).$

IR (film): v = 2943 s, 2866 s, 1582 m, 1477 m, 1464 m, 1117 m, 882 m, 791 m cm⁻¹.

¹H NMR (400 MHz, CDCl₃): δ = 7.53–7.50 (2H, m, Ph), 7.46–7.43 (2H, m, Ph), 7.33–7.23 (6H, m, Ph), 4.74 (1H, dd, J = 10.5, 4.1 Hz, H4), 4.16–4.11 (1H, m, H2), 3.70 (1H, dd,

J = 9.8, 3.7 Hz, $C1H_AH_B$), 3.50 (1H, dd, J = 9.8, 6.4 Hz, $C1H_AH_B$), 2.50 (1H, d, J = 4.8 Hz, OH), 2.09 (1H, ddd, J = 14.2, 9.9, 4.1 Hz, $C3H_AH_B$), 1.79 (1H, ddd, J = 14.2, 10.5, 3.1 Hz, $C3H_AH_B$), 1.07–0.99 (3H, m, SiCHMe₂), 1.03 (18H, d, J = 4.8 Hz, SiCHMe₂).

¹³C NMR (100 MHz, CDCl₃): δ = 134.3 (C, Ph), 134.0 (C, Ph), 133.0 (2CH, Ph), 132.7 (2CH, Ph), 129.1 (4CH, Ph), 127.9 (CH, Ph), 127.8 (CH, Ph), 69.5 (C2H), 67.3 (C1H₂), 54.8 (C4H), 39.6 (C3H₂), 18.1 (6CH₃, SiCH*Me*₂), 12.0 (3CH, Si*C*HMe₂).

LRMS (CI mode, NH₃): $m/z = 480.0 [(M + NH_4)^+, 3\%],$ 370.1 (23), 335.1 (100), 174.1 (9).

(4*R*,6*S*)-2,2-Dimethyl-4-tributylstannyl-6-triisopropylsilyloxymethyl-1,3-dioxane (26)

Lithium 4,4'-di-tert-butylbiphenylide (LDBB) was prepared by a modification to the method of Freeman and Hutchinson:³⁶ a mixture of Li (3.24 g, 467 mmol), 4,4'-di-tert-butylbiphenyl (12.5 g, 46.7 mmol) and THF (160 mL) was stirred at 0 °C for 48 h under a static Ar atmosphere. The LDBB solution was added dropwise to a solution of sulfides 23a and 23b (4.42 g, 10.8 mmol) in THF (120 mL) at -78 °C and the resulting dark blue solution stirred at -78 °C for 10 min before the addition of Bu₃SnCl (3.3 mL, 11.3 mmol) dropwise. After stirring for 10 min, H₂O (100 mL) and Et₂O (100 mL) were added and the cold bath removed. The phases were separated and the aqueous phase was extracted with Et₂O (3×50 mL). The combined organic phases washed with NaOH (0.5 M, 3 × 50 mL), dried, filtered and concentrated in vacuo. The residue was purified by column chromatography (SiO₂, hexanes \rightarrow ether : hexanes = 1:99) to give the title compound (4.96 g, 8.38 mmol, 81%) as a colourless oil. ¹³C NMR spectroscopy indicated the presence of a single isomer, identified as the expected *trans*-disubstituted 1,3-dioxane by reference to the chemical shifts of the acetonide methyl signals.^{66,67} Compound 26 has been previously described, with only the following ¹³C NMR spectroscopic data reported: $\delta = 24.7$ (Me), 24.5 (Me) ppm.⁶⁶

 $[a]_{\rm D} = -17.2 \ (c \ 1.02, \ \text{CHCl}_3).$

IR (film): v = 2949 s, 2928 s, 2870 s, 1465 m, 1382 m, 1225 m, 1143 m, 1101 m, 1002 m, 878 m, 692 m cm⁻¹.

¹H NMR (400 MHz, CDCl₃): δ = 4.20 (1H, dd, J = 11.3, 6.3 Hz, C4H), 3.90 (1H, dq, J = 8.8, 5.9 Hz, C6H), 3.75 (1H, dd, J = 10.0, 5.8 Hz, CH_AH_BOTIPS), 3.62 (1H, dd, J = 10.0, 5.8 Hz, CH_AH_BOTIPS), 2.11 (1H, dt, J = 5.9, 12.1 Hz, C5H_AH_B), 1.69 (1H, ddd, J = 12.7, 8.9, 6.2 Hz, C5H_AH_B), 1.58–1.46 (6H, m, SnCH₂CH₂CH₂CH₂Me), 1.36–1.26 (6H, m, SnCH₂CH₂CH₂Me), 1.32 and 1.29 (3H each, s, CMe₂), 1.13–1.05 (3H, m, SiCHMe₂), 1.07 (18H, d, J = 4.4 Hz, SiCHMe₂), 0.93–0.84 (15H, m, SnCH₂CH₂CH₂Me).

¹³C NMR (100 MHz, CDCl₃): δ = 100.4 (C2), 68.1 (C6H), 66.7 (CH₂OTIPS), 59.8 (C4H), 34.1 (C5H₂), 29.3 (3CH₂, ³J_{C-Sn} = 10.4, SnCH₂CH₂CH₂Me), 27.8 (3CH₂, ²J_{C-Sn} = 25.2, SnCH₂CH₂CH₂CH₂Me), 24.9 (CMe₂), 24.7 (CMe₂), 18.1 (6CH₃, SiCHMe₂), 13.9 (3CH₃, SnCH₂CH₂CH₂Me), 12.2 (3CH, SiCHMe₂), 8.8 (3CH₂, ¹J_{C-Sn} = 161.0, 150.9, SnCH₂CH₂-CH₂Me).

LRMS (EI⁺ mode): m/z = 591.2 [M⁺⁺, 0.1%], 535.2 (19), 477.2 (40), 291.1 (100), 243.2 (75), 157.1 (74), 115.0 (38).

Found: C, 56.90; H, 9.98. C₂₈H₆₀O₃SiSn requires: C, 56.85; H, 10.22%.

(4RS,6S)-4-Allyl-2,2-dimethyl-6-triisopropylsilyloxymethyl-1,3-dioxane (32a,b)

BuLi (0.15 mL of a 2.29 M solution in hexanes, 0.35 mmol) was added to a solution of stannane **26** (190 mg, 0.32 mmol) in THF (20 mL) at -78 °C under N₂. The solution was stirred at -78 °C for 5 min and then cooled to -90 °C. A solution of CuBr·SMe₂ (79 mg, 0.39 mmol) in diisopropyl sulfide (0.3 mL) and THF (0.3 mL) was added *via* cannula maintaining the

reaction temperature below -80 °C. The orange solution was stirred at -78 °C for 30 min before cooling to -90 °C and dropwise addition of a solution of complex 31 (which had been freshly prepared from neutral complex 17a (91 mg, 0.35 mmol) and NOBF₄ (45 mg, 0.39 mmol) in MeCN (4 mL), 0 °C, 20 min). The brown solution was allowed to warm to -78 °C over 30 min before addition of aqueous NH₃ (5 mL), aqueous NH₄Cl (10 mL) and Et₂O (25 mL) and removal of the cooling bath. After warming to room temperature, the mixture was filtered through Celite, rinsing with Et₂O (3×25 mL). The phases were separated, the aqueous phase was extracted with Et_2O (3 × 25 mL) and the combined organic phases were washed with brine (50 mL), dried, filtered and concentrated in vacuo. The crude products were dissolved in analytical grade chloroform (50 mL), and stirred at rt with a stream of O₂ bubbling through the solution for 17 h. The solvent was removed in vacuo and the residue purified by column chromatography (SiO₂, Et_2O : hexanes = 2:98) to give the title compound (53 mg, 0.15 mmol, 48%) as a colourless oil. ¹H NMR spectroscopy indicated that olefin 32a,b was present as a mixture of epimers (inseparable by column chromatography) at the C4 position. The major isomer was determined to be the (6S)epimer by the large $({}^{3}J 11.6)$ coupling of H6 to H5 (C₆D₆). ${}^{13}C$ NMR spectroscopic data confirmed the assignment, acetonide methyl carbon shifts at 30.2 and 20.0 ppm being indicative of the stereochemistry.^{66,67} The minor (6R)-isomer exhibited acetonide methyl carbon shifts at 25.2 ppm (2C, 3). The ratio of equatorial : axial isomers was estimated from ¹H NMR spectroscopy (CDCl₃) comparing the integration of signals at: 3.79-3.72 (2 overlapping dd, 1 each from (6R)- and (6S)isomers) and 3.63 (1H, dd, (6R)-isomer).

 $[a]_{\rm D} = -12.8 \ (c \ 1.06, \ {\rm CHCl}_3).$

IR (film): v = 2943 s, 2866 s, 1642 w, 1464 m, 1379 m, 1261 m, 1200 m, 1172 m, 1114 s, 994 m, 883 m cm⁻¹.

(6*S*)-isomer only ¹H NMR (400 MHz, C_6D_6): $\delta = 5.90-5.80$ (1H, m, $CH=CH_2$), 5.06–5.01 (2H, m, $CH=CH_2$), 3.88 (1H, ddt, J = 11.6, 2.5, 5.5 Hz, C4H), 3.80 (1H, dd, J = 9.7, 5.2 Hz, CH₂OTIPS), 3.69 (1H, ddt, J = 11.6, 2.4, 6.0 Hz, C6H), 3.57 (1H, dd, J = 9.7, 2.2 Hz, CH₂OTIPS), 2.34–2.27 (1H, m, CH_AH_BCH=CH₂), 2.14–2.07 (1H, m, CH_AH_BCH=CH₂), 1.45 (1H, dt, J = 12.8, 2.6 Hz, C5H_AH_B), 1.30 (3H, s, Me_ACMe_B), 1.26–1.17 (1H, m, C5H_AH_B), 1.11 (18H, d, J = 2.8 Hz, SiCHMe₂), 1.15–1.08 (3H, m, SiCHMe₂).

(6*S*)-isomer (major) ¹³C NMR (100 MHz, CDCl₃): $\delta = 134.4$ (*C*H=CH₂), 117.2 (CH=CH₂), 98.6 (*C*Me₂), 70.2 (C4H), 68.7 (C6H), 67.4 (CH₂OTIPS), 41.1 (*C*H₂CH=CH₂), 33.9 (C5H₂), 30.2 (*Me*_ACMe_B), 20.0 (Me_AC*Me*_B), 18.1 (6CH₃, SiCH*Me*₂), 12.2 (3CH, SiCHMe₂).

(6*R*)-isomer (minor) ¹³C NMR (100 MHz, CDCl₃): $\delta = 134.7$ (*C*H=CH₂), 117.0 (CH=CH₂), 100.3 (*C*Me₂), 68.1 (C6H or C4H), 66.7 (CH₂OTIPS), 66.5 (C6H or C4H), 40.4 (*C*H₂CH=CH₂), 34.4 (C5H₂), 25.2 (2C, *CMe₂*), 18.1 (6CH₃, SiCH*Me₂*), 12.2 (3CH, SiCHMe₂).

LRMS (CI⁺ mode): *m*/*z* = 343.2 [(M + H)⁺, 5], 285.2 (100), 267.2 (26), 241.2 (20), 217.2 (7), 173.1 (13), 111.1 (32).

Found: C, 66.75; H, 11.09. C₁₉H₃₈O₃Si requires: C, 66.61; H, 11.18%.

(2*R*,4*R*,6*S*)-2-Phenyl-4-tributylstannanyl-6-triisopropylsilyloxymethyl-1,3-dioxane (33a) and (2*S*,4*R*,6*S*)-2-phenyl-4-tributylstannanyl-6-triisopropylsilyloxymethyl-1,3-dioxane (33b)

To a solution of stannane **26** (4.32 g, 7.30 mmol), methanol (0.9 mL, 21.9 mmol) and benzaldehyde dimethylacetal (5.5 mL, 36.5 mmol) in CH₂Cl₂ (120 mL) at rt under N₂ was added *p*-TsOH (69 mg, 0.37 mmol). The solution was stirred at rt for 7 h before concentration *in vacuo*. The residue was purified by column chromatography (SiO₂, Et₂O : hexanes = 2 : 98) to give the title compounds (4.17 g, 6.52 mmol, 89%) as a colourless oil. ¹H NMR spectroscopy indicated a mixture of **33a** and **33b**

in the approximate ratio 7 : 1, based on the integration of C2H singlets at 5.81 and 5.73 ppm respectively. Separation of isomers was possible by careful column chromatography (SiO₂, PhMe : hexanes = 1 : 3). The major isomer was identified as the (2R)-isomer **33a** by NOE studies.

Data for the (2*R*)-isomer (**33a**): ($R_f = 0.13$, PhMe : hexanes = 1 : 3)

 $[a]_{\rm D} = +20.6 \ (c \ 1.61, \ {\rm CHCl}_3).$

IR (film): v = 2922 s, 2860 s, 1460 m, 1107 m, 755 m, 687 m cm⁻¹.

¹H NMR (400 MHz, C_6D_6): $\delta = 7.93-7.90$ (2H, m, Ph), 7.36-7.22 (3H, m, Ph), 5.81 (1H, s, C2H), 5.15 (1H, apparent d, J = 6.4 Hz, C4H), 4.26 (1H, dddd, J = 10.7, 6.9, 5.2, 2.4 Hz, C6H), 4.18 (1H, dd, J = 9.7, 5.0 Hz, CH_AH_BOTIPS), 3.89 (1H, dd, J = 9.7, 7.2 Hz, CH_AH_BOTIPS), 2.56 (1H, ddd, J = 13.3, 10.8, 6.4 Hz, $C5H_AH_B$), 2.07 (1H, br dd, J = 13.3, 1.4 Hz, $C5H_AH_B$), 1.76–1.63 (6H, m, SnCH₂CH₂CH₂Me), 1.49 (6H, sextet, J = 7.3 Hz, SnCH₂CH₂CH₂Me), 1.27–1.12 (12H, m, SnCH₂CH₂CH₂Me + SiCHMe₂), 1.22 (18H, d, J = 2.8 Hz, SiCHMe₂), 1.04 (6H, t, J = 7.2 Hz, SnCH₂CH₂CH₂Me).

¹³C NMR (100 MHz, CDCl₃): δ = 139.1 (C, Ph), 128.8 (CH, Ph), 128.4 (2CH, Ph), 126.2 (2CH, Ph), 100.6 (C2H), 77.4 (C6H), 74.4 (C4H), 66.6 (CH₂OTIPS), 33.9 (C5H₂), 29.3 (3CH₂, ³J_{C-Sn} = 10.2, SnCH₂CH₂CH₂Me), 27.7 (3CH₂, ²J_{C-Sn} = 27.8, SnCH₂CH₂CH₂Me), 18.2 (6CH₃, SiCHMe₂), 13.8 (3CH₃, Sn(CH₂)₃Me), 12.1 (3CH, SiCHMe₂), 10.3 (3CH₂, ¹J_{C-Sn} 150.1, 143.6, SnCH₂CH₂CH₂Me).

LRMS (CI⁺ mode): *m*/*z* = 641.2 [(M + H)⁺, 35], 583.1 (100), 581.1 (76), 533.2 (32), 475.1 (18), 291.1 (44), 289.1 (34), 243.2 (22), 107.1 (86).

Found: C, 60.17; H, 9.41. C₃₂H₆₀O₃SiSn requires: C, 60.09; H, 9.46%.

Data for the (2*S*)-isomer (**33b**): ($R_f = 0.22$, PhMe : hexanes = 1 : 3).

 $[a]_{\rm D} = -2.14 \ (c \ 1.54, \ {\rm CHCl}_3).$

IR (film): v = 2960 s, 2864 s, 1460 s, 1380 m, 1114 m, 1073 m, 1018 m, 881 m, 798 m cm⁻¹.

¹H NMR (400 MHz, CDCl₃): δ = 7.46–7.44 (2H, m, Ph), 7.36–7.28 (3H, m, Ph), 5.73 (1H, s, C2H), 4.59 (1H, dd, *J* = 13.7, 2.3 Hz, C4H), 4.35 (1H, t, *J* = 9.0 Hz, CH_AH_BOTIPS), 4.17–4.12 (1H, m, C6H), 4.01 (1H, dd, *J* = 9.5, 5.2 Hz, CH_AH_B-OTIPS), 2.59 (1H, dt, *J* = 6.1, 13.8 Hz, C5H_AH_B), 1.85 (1H, ddd, *J* = 13.8, 2.3, 1.1 Hz, C5H_AH_B), 1.61–1.51 (6H, m, SnCH₂CH₂CH₂Me), 1.31 (6H, sextet, *J* = 7.2 Hz, SnCH₂CH₂-CH₂Me), 1.18–1.08 (3H, m, SiCHMe₂), 1.10 (18H, d, *J* = 5.2 Hz, SiCHMe₂), 0.99–0.94 (6H, m, SnCH₂CH₂CH₂Me), 0.90 (9H, t, *J* = 7.4 Hz, SnCH₂CH₂Me).

¹³C NMR (100 MHz, CDCl₃): δ = 140.0 (C, Ph), 128.5 (CH, Ph), 128.2 (2CH, Ph), 126.2 (2CH, Ph), 97.9 (C2H), 73.1 (C4H), 68.1 (C6H), 61.8 (CH₂OTIPS), 30.1 (C5H₂), 29.3 (3CH₂, ³J_{C-Sn} = 10.2 Hz, SnCH₂CH₂CH₂Me), 27.9 (3CH₂, ²J_{C-Sn} = 26.8 Hz, SnCH₂CH₂CH₂Me), 18.2 (6CH₃, SiCHMe₂), 13.9 (3CH₃, Sn(CH₂)₃Me), 12.1 (3CH, SiCHMe₂), 8.6 (3CH₂, ¹J_{C-Sn} = 160.6, 153.6 Hz, SnCH₂CH₂CH₂Me).

LRMS (CI⁺ mode): m/z = 641.0 [(M + H)⁺, 49%], 583.0 (100), 581.0 (75), 533.0 (31), 351.1 (42), 291.0 (69), 289.0 (53).

Found: C, 60.07; H, 9.36. C₃₂H₆₀O₃SiSn requires: C, 60.09; H, 9.46%.

(2*S*,4*R*,6*S*)-4-Allyl-2-phenyl-6-triisopropylsilyloxymethyl-1,3-dioxane (34)

Olefin 34 was prepared in an analogous fashion to olefin 32 on a scale of 0.25 mmol of stannane 33a and 0.28 mmol of neutral complex 31. Purification by column chromatography (SiO₂, Et₂O : hexanes = 3 : 97) gave the title compound (50 mg, 0.13 mmol, 51%) as a clear oil. ¹H and ¹³C NMR spectroscopy indicated the presence of a single isomer, identified as the (6*S*)-isomer on the basis of the small (J = 6.9) coupling between C6H and C5H. NOE experiments confirmed the assignment, with

large (12–16%) enhancements observed between C6H and C2H, and no enhancement observed between C4H and C6H when either position was irradiated.

 $[a]_{\rm D} = +17.5 \ (c \ 0.59 \ {\rm CHCl}_3).$

IR (film): v = 2866 s, 1463 m, 1383 m, 1216 m, 1118 s, 1069 m, 1027 m, 995 s, 918 m, 883 s, 754 s, 697 m cm⁻¹.

¹H NMR (400 MHz, CDCl₃): δ = 7.51–7.48 (2H, m, Ph), 7.38–7.30 (3H, m, Ph), 5.88 (1H, ddt, *J* = 16.8, 10.0, 7.3 Hz, CH=CH₂), 5.84 (1H, s, C2H), 5.21–5.13 (2H, m, CH=CH₂), 4.35 (1H, m, apparent q, *J* = 6.9 Hz, C6H), 4.18 (1H, ddt, *J* = 11.0, 2.5, 5.9 Hz, C4H), 3.93 (1H, dd, *J* = 9.9, 5.4 Hz, CH_AH_BOTIPS), 3.69 (1H, dd, *J* = 9.9, 6.4 Hz, CH_AH_BOTIPS), 2.87 (1H, dt, *J* = 14.4, 7.3 Hz, CH_AH_BCH=CH₂), 2.55 (1H, dt, *J* = 14.4, 7.3 Hz, CH_AH_BCH=CH₂), 2.00 (1H, ddd, *J* = 13.8, 11.2, 6.2 Hz, C5H_AH_B), 1.74 (1H, ddd, *J* = 13.5, 2.5, 1.3 Hz, C5H_AH_B), 1.15–1.03 (3H, m, SiCHMe₂), 1.08 (18H, d, *J* = 5.2 Hz, SiCHMe₂).

¹³C NMR (100 MHz, CDCl₃): δ = 139.1 (C, Ph), 134.7 (CH=CH₂), 128.8 (CH, Ph), 128.3 (2CH, Ph), 126.3 (2CH, Ph), 117.6 (CH=CH₂), 94.4 (CHPh), 73.2 (C4H), 72.3 (C6H), 66.9 (CH₂OTIPS), 35.6 (CH₂CH=CH₂), 30.3 (C5H₂), 18.2 (6CH₃, SiCH*M*e₂), 12.1 (3CH, SiCHMe₂).

LRMS (CI⁺ mode): m/z = 391.1 [(M + H)⁺, 100], 347.1 (8), 285.1 (50), 261.1 (11), 241.1 (11), 111.1 (13), 107.1 (12).

Found: C, 70.65; H, 9.73. C₂₃H₃₈O₃Si requires: C, 70.72; H, 9.81%.

(2*S*,4*S*,6*S*)-4-[(1*R*,2*E*)-1-Methyl-3-phenyl-2-propenyl]-2-phenyl-6-triisopropylsilyloxymethyl-1,3-dioxane (6) and (2*S*,4*S*,6*S*)-4-[(1*S*,2*E*)-1-phenyl-2-butenyl]-2-phenyl-6-triisopropylsilyloxymethyl-1,3-dioxane (35)

n-BuLi (5.4 mL of a 1.7 M solution in hexanes) was added dropwise to a solution of stannane 33a (5.40 g, 8.45 mmol) in THF (150 mL) at -80 °C under N₂. After the light-yellow solution was stirred at -80 °C for 1 h, a solution of CuBr·SMe₂ (2.08 g, 10.14 mmol) in di-iso-propylsulfide (7 mL) and THF (8.5 mL) was added via cannula, maintaining the internal solution temperature below -80 °C. The orange-brown solution was stirred at -80 °C for 1 h under N₂ before the addition of cationic complex 7 (freshly prepared: nitrosonium tetrafluoroborate (1.28 g, 11.0 mmol) was added to a solution of neutral complex 15 (3.53 g, 10.1 mmol, prepared by procedure A above) in MeCN (20 mL) at 0 °C and the yellow solution stirred at 0 °C under N₂ for 15 min) via cannula. The light-brown solution was stirred at -80 °C for 1 h before the addition of aqueous NH₄Cl (40 mL) and aqueous NH₃ (10 mL) and removal of the cooling bath. After reaching room temperature, the mixture was filtered through Celite, washing thoroughly with Et₂O (50 mL). The phases were separated, and the aqueous phase extracted with Et₂O (2×50 mL), and the combined organic phases washed with brine (100 mL), dried, filtered and concentrated in vacuo. The crude material was dissolved in CHCl₃ (250 mL) and stirred at rt for 17 h with a stream of O₂ bubbling through the brown solution. Removal of solvent in vacuo yielded a dark brown oil which was purified by column chromatography (SiO₂, Et_2O : hexanes = 2:98) to give a mixture of the title compounds (2.90 g, 6.03 mmol, 71% from stannane 33a) as a pale yellow oil. ¹H NMR spectroscopy revealed a ratio of 6:35 of approximately 1.2:1 (in favour of the desired isomer), estimated by integration of the vinylic proton peaks at 6.51 and 6.28 ppm (6) and 5.64–5.50 ppm (35). $[a]_{\rm D}$ (1.2 : 1 mixture of **6** : **35**) = +23.3 (c 1.50, CHCl₃).

IR (film) v = 2942 s, 2866 s, 1462 m, 1117 s, 1069 m, 1028 m, 1014 m, 995 m, 882 m, 748 m, 696 s, 660 m cm⁻¹.

¹H NMR (400 MHz, CDCl₃): δ = 7.53–7.17 (19H, m, Ph), 7.05–7.04 (1H, m, Ph), 6.51 [1H, d, *J* = 15.9 Hz, PhCH=CHR, (6)], 6.28 [1H, dd, *J* = 15.9, 8.4 Hz, PhCH=CHR, (6)], 5.85 [1H, s, CHPh, (6)], 5.76 [1H, s, CHPh, (35)], 5.64–5.50 [2H, m, MeCH=CHR, (35)], 4.44 [1H, dd, *J* = 11.1, 5.0 Hz, (35)], 4.27– 3.90 (6H, m), 3.72 [2H, ddd, J = 10.0, 6.6, 1.4 Hz, (**6**)], 3.19 (1H, q, J = 8.3 Hz), 2.11 [1H, ddd, J = 13.5, 2.5, 1.5 Hz, (**35**)], 2.02–1.90 (3H, m), 1.66 [3H, dd, J = 5.6, 0.8 Hz, (**35**)], 1.13 [3H, d, J = 6.4 Hz, Me (**6**)], 1.12–1.00 (42H, m, SiCHMe₂).

¹³C NMR (100 MHz, CDCl₃): δ = 141.9 (C, Ph), 139.1 (C, Ph), 138.9 (C, Ph), 137.8 (C, Ph), 133.5 [PhCH=*C*HR (6)], 132.2 [*C*H=CH, (**35**)], 130.1 [PhCH=CHR (6)], 128.8 (2CH, Ph), 128.7 (2CH, Ph), 128.6 [CH, Ph or CH=CH, (**35**)], 128.4 [CH, Ph or CH=CH, (**35**)], 128.3 (2CH, Ph), 128.2 (2CH, Ph), 128.1 (2CH, Ph), 127.9 [CH, Ph or CH=CH, (**35**)], 127.2 [CH, Ph or CH=CH, (**35**)], 126.6 [CH, Ph or CH=CH, (**35**)], 126.3 (2CH, Ph), 126.2 (2CH, Ph), 125.9 (2CH, Ph), 94.8 [CHPh (6)], 94.3 [CHPh, (**35**)], 76.6 (CH), 74.8 (CH), 73.3 (CH), 73.1 (CH), 66.8 (2CH₂), 50.0 (CH), 37.6 [PhCH=CHCHMeR, (6)], 28.9 (CH₂), 28.7 (CH₂), 18.2 (14CH₃, Me + SiCH*Me*₂), 12.2 (6CH, SiCHMe₂).

LRMS (CI mode, isobutane): m/z = 481 [(M + H)⁺, 17%], 393 (21), 375 (58), 351 (100), 307 (25), 245 (44).

Found: C, 74.86; H, 9.41. C₃₀H₄₄O₃Si requires: C, 74.95; H, 9.22%.

(2*R*,4*S*,5*R*,6*E*)-5-Methyl-7-phenyl-hept-6-ene-1,2,4-triol (38) and (2*R*,4*S*,5*S*,6*E*)-5-phenyl-oct-6-ene-1,2,4-triol (39)

To a solution of dioxanes **6** and **35** (**6** : **35** = 1.2 : 1, 2.77 g, 5.76 mmol) in MeOH (100 mL) at rt was added *p*-toluenesulfonic acid monohydrate (164 mg, 0.86 mmol). The pale yellow solution was stirred at rt for 1 d before solvent removal *in vacuo*. The residue was purified by column chromatography (SiO₂, EtOAc) to give a mixture of the title compounds (861 mg, 3.64 mmol, 63%) as a pale yellow oil. Careful repetitive column chromatography allowed the separation of isomers. Triol **38**, a viscous oil, gave : $[a]_{\rm D} = +103.6$ (*c* 1.10, MeOH).

IR (film): v = 3465 br s, 2935 m, 2873 m, 1452 m, 1388 m, 1365 m, 1329 m, 1082 m, 992 m, 972 m cm⁻¹.

¹H NMR (400 MHz, CDCl₃): δ = 7.38–7.23 (5H, m, Ph), 6.49 (1H, d, J = 16.1 Hz, C7H), 6.12 (1H, dd, J = 16.1, 8.7 Hz, C6H), 4.05–3.99 (1H, m, C2H), 3.80–3.76 (1H, m, C4H), 3.67 (1H, dd, J = 11.1, 3.6 Hz, C1 H_AH_B), 3.54 (1H, dd, J = 11.1, 7.0 Hz, C1H_A H_B), 2.41 (1H, br sextet, J = 7.3 Hz, C5H), 1.75 (1H, ddd, J = 14.4, 8.7, 2.5 Hz, C3 H_AH_B), 1.60 (1H, ddd, J = 14.4, 9.3, 3.5 Hz, C3H_A H_B), 1.12 (3H, d, J = 6.8 Hz, C5–Me).

¹³C NMR (100 MHz, CDCl₃): δ = 137.1 (C, Ph), 132.3 (C6H or C7H), 131.6 (C6H or C7H), 128.8 (2CH, Ph), 127.7 (CH, Ph), 126.4 (2CH, Ph), 72.3 (C2H), 69.6 (C4H), 66.9 (C1H₂), 44.2 (C5H), 36.4 (C3H₂), 16.9 (C5–*Me*).

LRMS (CI mode, NH₃): $m/z = 254.2 [(M + NH_4)^+, 100\%]$, 237.1 (28), 219.1 (22).

Found: C, 71.15; H, 8.70. $C_{14}H_{20}O_3$ requires: C, 71.16; H, 8.53%.

Triol **39** solidified upon standing and was recrystallised from Et_2O to give fine white needles, mp 110–111 °C.

 $[a]_{\rm D} = -69.1 \ (c \ 1.65, \ {\rm MeOH}).$

IR (KBr): v = 3397 br s, 1112 m, 1082 m, 1070 s, 1025 s, 963 m, 702 m cm⁻¹.

¹H NMR (400 MHz, CDCl₃): δ = 7.53–7.30 (2H, m, Ph), 7.26–7.17 (3H, m, Ph), 5.65–5.53 (2H, m, C6H and C7H), 4.13 (1H, dt, *J* = 2.5, 8.8 Hz, C4H), 4.07–4.01 (1H, m, C2H), 3.65 (1H, dd, *J* = 11.1, 3.5 Hz, C1*H*_AH_B), 3.53 (1H, dd, *J* = 11.1, 7.0 Hz, C1H_AH_B), 3.30 (1H, t, *J* = 8.2 Hz, C5H), 2.94 (1H, br s, OH), 2.18 (1H, br s, OH), 1.88 (1H, ddd, *J* = 14.5, 8.7, 2.6 Hz, C3*H*_AH_B), 1.68 (3H, d, *J* = 5.0 Hz, C8H₃), 1.63 (1H, br s, OH), 1.55 (1H, ddd, *J* = 14.5, 9.1, 3.5 Hz, C3H_AH_B).

¹³C NMR (100 MHz, CDCl₃): δ = 141.4 (C, Ph), 130.8 (Ph, C6H or C7H), 129.2 (2CH, Ph), 128.5 (2CH, Ph), 128.4 (Ph, C6H or C7H), 127.2 (Ph, C6H or C7H), 72.1 (C4H), 69.7 (C2H), 67.1 (C1H₂), 56.7 (C5H), 36.8 (C3H₂), 18.3 (C8H₃).

LRMS (CI mode, NH₃): m/z = 254.2 [(M + NH₄)⁺, 100%], 236.2 (30), 219.2 (8), 116.1 (12).

Found: C, 71.27; H, 8.73. $C_{14}H_{20}O_3$ requires: C, 71.16; H, 8.53%.

(2*E*,5*S*,6*R*,7*E*)-5-Hydroxy-6-methyl-8-phenylocta-2,7-dienoic acid methyl ester (5)

To a solution of triol 38 (125 mg, 0.53 mmol) in MeOH (15 mL) and H₂O (5 mL) at rt was added sodium periodate (170 mg, 0.79 mmol). The clear solution was stirred at rt for 1.5 h, after which time a white precipitate was present. Methanol was removed in vacuo and H₂O (30 mL) and CH₂Cl₂ (20 mL) were added. The phases were separated and the aqueous phase extracted with CH_2Cl_2 (2 × 20 mL). The combined organic phases were dried, filtered and concentrated in vacuo to afford a crude aldehyde as a colourless oil (103 mg, 0.50 mmol). The crude aldehyde was twice dissolved in PhMe (20 mL) and the solvent evaporated. To a solution of the crude aldehyde in THF (17 mL) was added trimethylphosphonoacetate (0.17 mL, 1.17 mmol) and the mixture cooled to -78 °C under N₂ whereupon N, N, N', N'-tetramethylguanidine (0.15 mL, 1.17 mmol) in THF (5 mL) was added dropwise over 2 min. The clear solution was allowed to warm to rt over 16 h and stirred at rt for 42 h before the addition of H₂O (20 mL) and Et₂O (20 mL). The phases were separated and the aqueous phase was extracted with Et₂O (3×25 mL). The combined organic phases were dried, filtered and concentrated in vacuo to afford a pale yellow oil. The residue was purified by column chromatography (SiO₂, Et₂O : cyclohexane = 2 : 8 \rightarrow 4 : 6) to give the title compound (114 mg, 0.44 mmol, 83%) as a colourless oil. $[a]_{\rm D} = +71.7$ (*c* 1.20, CHCl₃); lit. $[a]_{\rm D} = +55.2$ (*c* 0.31, CHCl₃)⁴¹ Spectroscopic data were in accordance with literature data.41

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