PERKIN 1

Enantiospecific syntheses of pseudopterosin aglycones. Part 1. Synthesis of the putative aglycone of pseudopterosin G–J *via* an A→AB→ABC annulation strategy

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The putative aglycone of pseudopterosin G–J and its enantiomer were synthesised enantiospecifically from 2,3-dimethoxytoluene and η^3-allyl cationic complexes of molybdenum and iron respectively. The A⟶AB⟶ABC annulation strategy entailed the use of allyl cations or their equivalents for the creation of the three benzylic stereogenic centres. The X-ray structure of tetrahydronaphthalene (−)-**41a** was determined

Introduction

Gorgonian soft corals are abundant in the warm, nutrient-rich reefs and shallow waters of the Caribbean Sea. Nature's largesse extends to the deeper waters too for it is there, at depths of 35 meters or so, that the sea whip *Pseudopterogorgia elisabethae* may be found. *P. elisabethae* attracted attention in 1982 when routine screening revealed the presence of cytotoxic metabolites with antimicrobial activity. A subsequent mass collection, extraction and fractionation of *P. elisabethae* led to the isolation of the first four members of an extended family of metabolites which were named the pseudopterosins.[1,2] The most abundant member of the family, pseudopterosin C underwent extensive chemical and spectroscopic scrutiny and its structure was firmly established by X-ray crystallography. Further study established that all four members of the family were β-xylopyranosides of the same hexahydro-1*H*-phenalene core as depicted in structures **1A**–**D** (Scheme 1).

Pseudopterosin A revealed potent anti-inflammatory and analgesic activity *in vivo* (see below) which stimulated the search for further members of the family. *Seco*-pseudopterosins A–D (**2**) isolated from *Pseudopterogorgia kallos* were identified as β-arabinopyranosides with a common serrulatane core and they too possessed notable anti-inflammatory activity.[3] Then in 1990 a further batch of 8 new pseudopterosins from fresh extracts of *P. elisabethae* were isolated.[4] Rodríguez and co-workers[5] isolated 4 unusual terpenes† with novel skeletons related to the pseudopterosins from the same source and recently a routine screen for antitubercular compounds from extracts of *P. elisabethae* discovered pseudopteroxazole (**3**) and *seco*-pseudopteroxazole (**4**).[6] Pseudopteroxazole is a potent growth inhibitor of *Mycobacterium tuberculosis* H37Rv whilst *seco*-pseudopteroxazole shows moderate to strong inhibition. Finally, the blue coral *Heliopora coerulea* produces diterpene metabolites helioporins A–G closely related to the pseudopterosins.[7] ‡ A noteworthy feature of the pseudopterosin family is the stereochemical variation in the hexahydro-1*H*-phenalene core. Thus the first six members (A–F) of the family share the same diterpene aglycone **5** whereas the next four (G–J) were believed to be epimeric at C6 (*i.e.* structure **6**). The aglycone **7** of pseudopterosins K and L, on the other hand, is enantiomeric to that of A–F.

The anti-inflammatory and analgesic activity of the pseudopterosins has been ascribed to the inhibition of eicosanoid release. Experiments with pseudopterosins A and E led to the conclusion that the *ortho*-quinone **8** derived from oxidation of the aglycone **5** is the active agent. The glycosides are active in mice and in whole cells, but in crude enzyme preparations, they require the presence of fucosidase, suggesting that cleavage of the sugar is required for activity.[8,9]

The biological activity and commercial potential[10] of the pseudopterosins stimulated a number of approaches to their synthesis (Scheme 2). Total syntheses of pseudopterosins A and E have been described[11,12] but the bulk of the synthetic effort has focused on the aglycone. Most of the strategies reported to date begin with ring B in the form of the monoterpenes (+)-menthol (**10**),[12] (−)-limonene (**11**),[11,13] or (−)-isopulegol (**12**),[14] followed by construction of the arene (ring A) and finally ring C. One approach involves the same B⟶BA⟶BAC annulation sequence in which the B ring is constructed from an acyclic monoterpene precursor (−)-citronellal (**13**).[15] Buszek and Bixby began with (*R*)-(−)-2-phenylpropionic acid (**14**)[16] in which the stereogenic centre at C3 is fixed in the starting material. Two further approaches depart from the common path and follow an AB⟶ABC annulation sequence.[17,18] Both of these approaches begin with a tetralone (**15** or **16**) and both are essays in controlling benzylic stereochemistry. In addition several approaches to the tricyclic ring system in varying degrees of elaboration have been published.[19–25] We now give full details[26] of a rare A⟶AB⟶ABC strategy towards pseudopterosin G–J aglycone beginning with 2,3-dimethoxytoluene which proves that the stereochemistry assigned to the natural

† The four metabolites, elisabethins A–C and elisabanolide, were screened for biological activity. None of the compounds showed topical anti-inflammatory activity but elisabethin B displayed antitumour activity. Elisabethin C and elisabanolide showed modest antitubercular activity.[5]

‡ Helioporins A and B were inactive in topical anti-inflammatory assays but they exhibited activity against *Herpes simplex* type-1 virus whilst helioporins C–G were cytotoxic towards murine P388 lymphomas.[7]

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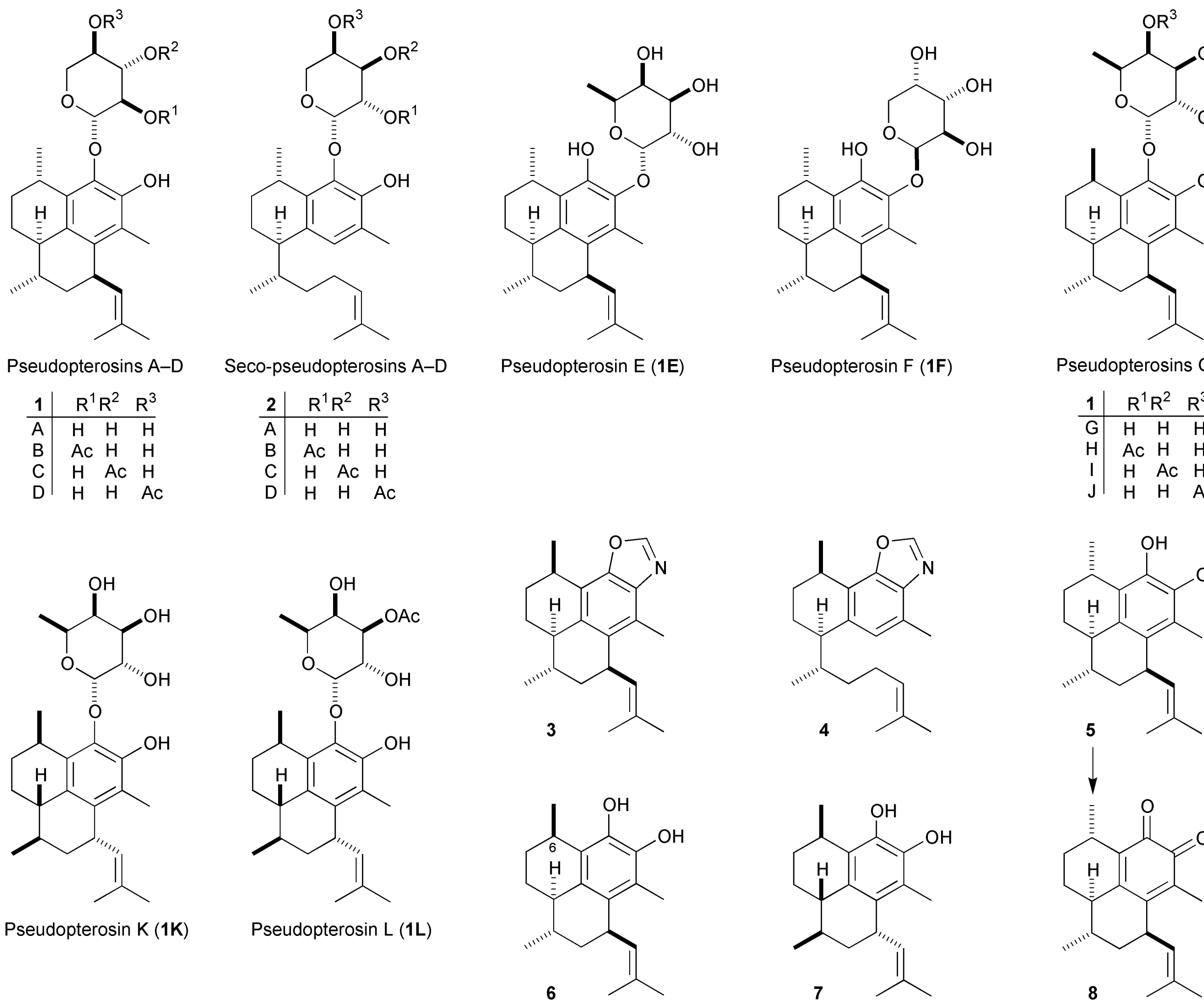
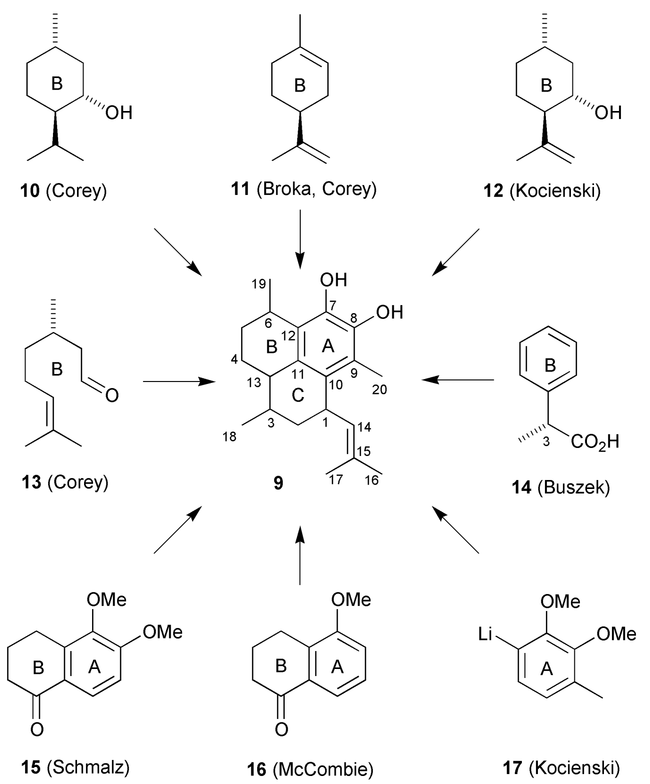


1	R1	R2	R3
A	H	H	H
B	Ac	H	H
C	H	Ac	H
D	H	H	Ac

2	R1	R2	R3
A	H	H	H
B	Ac	H	H
C	H	Ac	H
D	H	H	Ac

1	R1	R2	R3
G	H	H	H
H	Ac	H	H
I	H	Ac	H
J	H	H	Ac

Scheme 1



Scheme 2

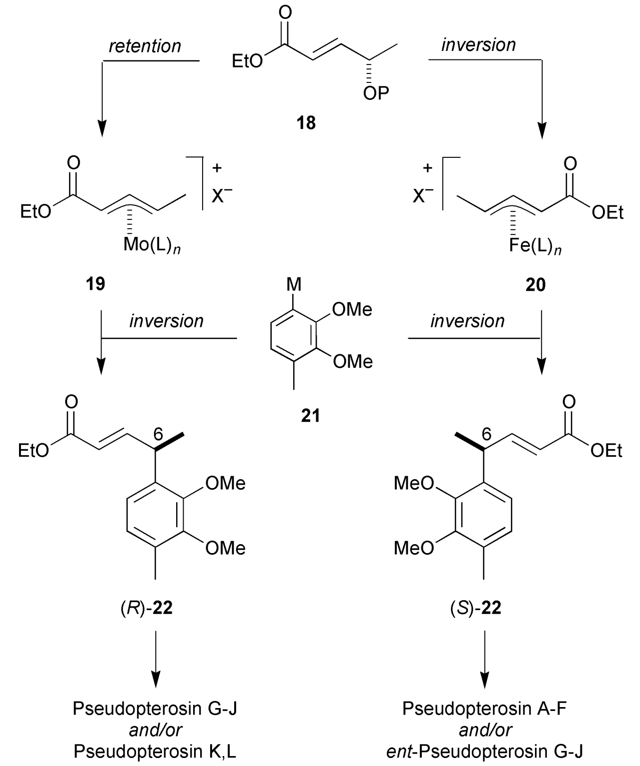
product is incorrect. In the accompanying paper we describe syntheses of the enantiomeric pseudopterosin A–F and K–L aglycones based on the B⟶BA⟶BAC annulation sequence.

Results and discussion

Plans and precedents

One of the major challenges posed by our adoption of an A⟶AB⟶ABC annulation strategy is that all four stereogenic centres—three of them benzylic—reside in rings B and C; therefore all four would have to be created. In order to give our strategy some coherence, we chose to create the three benzylic stereogenic centres using allylic cations, or their equivalents, in the sequence C6 then C13 and finally C1. An important consequence of beginning with C6 is that in principle, all members of the pseudopterosin family could be prepared from an enantiomeric pair of reagents and greatest economy would be achieved if that enantiomeric pair were created from a common starting material. A sequence which satisfies the foregoing conditions is depicted in Scheme 3. The salient feature of this sequence is the use of the η^3-allyl cationic complexes **19** and **20** whose reaction with the metallated 2,3-dimethoxytoluene derivative **21** would afford the enantiomers (*R*)-**22** and (*S*)-**22**.

There is ample precedent for the preparation of the ester-functionalised iron complex **20** from allyl alcohol precursor **18** with inversion of configuration and complex **20** is known to react with nucleophiles with inversion of configuration.[27,28] The regiochemistry of the reaction is also well precedented.[29–31]



Scheme 3

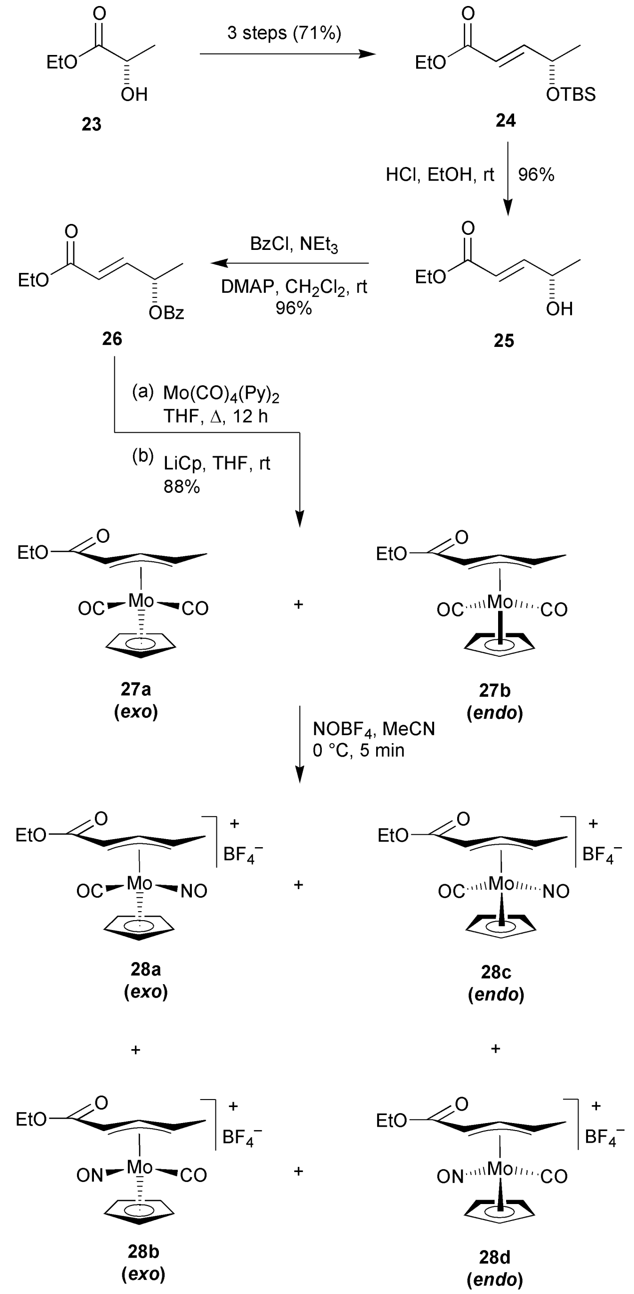
However, the precedent is less secure in the case of the molybdenum complex **19**. Whilst oxidative addition of Mo(0) to *unfunctionalised* allyl alcohol derivatives is known to occur with retention,[32] the effect of the ester function on the *reactivity* of substrate **18** was not known. Another cloud on the horizon concerns the regiochemistry of the reaction of complex **19** with **21**. Although the inversion of stereochemistry can be safely anticipated,[32,33] the factors governing regioselectivity are both complex and difficult to control.[34,35]

Construction of the C6 stereogenic centre

Our first task was the synthesis of the *functionalised* planar chiral η^3-allylmolybdenum cationic complex **28** (Scheme 4) which was to serve as the first allylic cation equivalent. Coming as it does at the beginning of the synthesis it was essential that an efficient and reliable method be secured using a readily available, enantiomerically pure starting material. We chose ethyl (*S*)-lactate (**23**), one of the cheapest chiral pool precursors currently available. It was transformed in three easy steps (71% overall) to the known[36] α,β-unsaturated ester **24** whereupon the TBS group was replaced by a benzoate ester **26** *via* alcohol **25**. An extended investigation of various known sources of Mo(0) for the oxidative addition was disappointing.[37] Success was eventually achieved by developing a new protocol involving a combination of $Mo(CO)_4(Py)_2$,§ THF as solvent and benzoate as leaving group. The desired oxidative addition took place efficiently under mild conditions with clean retention of stereochemistry. The resultant complex was then treated with lithium cyclopentadienide to deliver the required neutral complex **27a**,**b** as a mixture of *endo* and *exo* rotamers (*exo* : *endo* = 6 : 1)[38] in 88% overall yield. The rotamers were easily distinguished by NMR spectroscopy.¶ Unlike the majority of the simple alkyl-substituted complexes we have prepared, complex **27a**,**b** was unstable and decomposed on standing.

§ $Mo(CO)_4(Py)_2$ is easily prepared and used *in situ* by simply heating $Mo(CO)_6$ with 2 equiv. of pyridine in THF for 12 h.

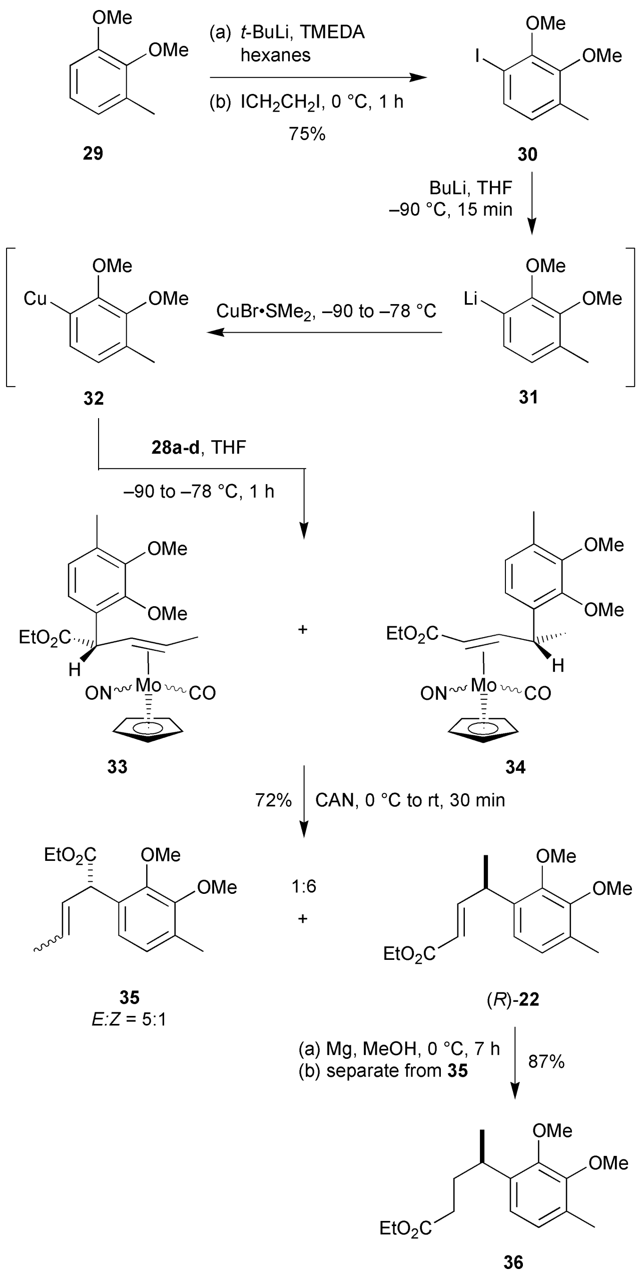
¶ The *endo* and *exo* rotamers equilibrate slowly at room temperature. Equilibration of the η^3-cyclooctenyl complex follows first-order kinetics with a rate constant $k_1 = 2 \times 10^{-4}$ s^{-1} ($\tau_{1/2}$ = 60 min) in acetonitrile at 25 °C.[34] However, the presence of *exo* and *endo* isomers is of little consequence since their rapid equilibration is catalysed by nucleophiles and the *exo* rotamer reacts much faster than the *endo* rotamer.[49,50]



Scheme 4

Conversion of the neutral complex **27a**,**b** to the electrophilic η^3-allyl cationic molybdenum complex was accomplished by ligand exchange with nitrosonium tetrafluoroborate in acetonitrile. The cationic complex, which is presumably a mixture of four diastereosiomers **28a**–**d** resulting from indiscriminate ligand exchange on **27a**,**b**, was generally used immediately in the next step. Attempts to characterise the cationic complex by NMR spectroscopy were hampered by its instability: even in the short time required to record the ^{1}H NMR spectrum, decomposition occurred.

The nucleophilic partner in the first stage of the synthesis was derived by metallation of commercial 2,3-dimethoxytoluene (**29**, Scheme 5) with *t*-BuLi in the presence of TMEDA at room temperature followed by iodination with 1,2-diiodoethane. When *s*-BuLi was used as the base, metallation required 50 °C in which case small amounts of inseparable by-products derived from competing metallation–iodination of the aryl methyl group were observed. The halogen–metal exchange on iodoarene **30** using *n*-BuLi followed by transmetallation with



Scheme 5

$CuBr{\cdot}SMe_2$ afforded the arylcopper(I) reagent **32** to which was added the freshly prepared η^3-allyl cationic molybdenum complex **28a–d** to give first the η^2-complexes **33** and **34**. Oxidative demetallation with ceric ammonium nitrate (CAN) then gave the alkylation products **35** and (*R*)-**22** (72% yield) in a ratio of 1 : 6 in favour of the desired isomer (*R*)-**22**. The alkylation products were not separable but treatment of the mixture with magnesium (10 equiv.) in MeOH at 0 °C, smoothly reduced the α,β-unsaturated isomer (*R*)-**22** to the saturated compound **36** which was then separated from the unwanted isomer **35** by column chromatography.

The stereochemistry and regiochemistry of the alkylation reaction deserves comment. At this stage of the synthesis we were not certain of the stereochemistry of **36** though reduction with lithium aluminium hydride followed by derivatisation as the Mosher ester established the er of the product as 97 : 3.‖ In order for the stereochemistry of **36** to be (*R*), the oxidative addition (**26** ⟶ **27a**,**b**) would have to occur with retention of configuration and the alkylation reaction (**32** + **28a–d** ⟶ **34**) with inversion. X-Ray crystallographic analysis of a subsequent product [(−)-**41a**, see below] confirmed the validity of the stereochemical assumptions for which, in any event, there was ample precedent.[32] Far less certain was the regiochemistry of the alkylation which is governed by three effects acting in opposition or reinforcement. Faller had shown that the stereochemistry at molybdenum, or more importantly, the location of the nitrosyl group, is a major determinant of the regiochemistry of alkylation with soft nucleophiles.[35] However, we had shown that the electronic effect of the nitrosyl group could be subverted by steric effects, at least in the case of organocopper(I) nucleophiles.[39,40] Finally, there is the electronic distortion caused by the presence of the ester function which, in the corresponding iron complexes (see below), is dominant.[27,41] Given the complexity of the factors involved together with the stereochemical ambiguity of the cationic complexes **28a–d**, we accepted the 1 : 6 ratio of regioisomers with grace if not with gusto.**

Construction of ring B

Construction of ring B was achieved by an intramolecular electrophilic aromatic substitution on the electron-rich dimethoxyarene using a propargyl (prop-2-ynyl) cation as the electrophile. The requisite propargylic precursor was synthesised in two steps from ester **36** (Scheme 6) by reduction with DIBAL-H followed by addition of (trimethylsilyl)ethynylmagnesium bromide to the aldehyde **37**. Attempts to cyclise the alcohols **38** (1 : 1 mixture of diastereoisomers) or the corresponding acetates with a variety of protic and Lewis acids were not fruitful: many products were formed which were difficult to separate. In order to tame the reactivity of the propargyl cation, the alkyne was converted to its dicobalt hexacarbonyl complex **39** and cyclisation induced by treatment with $BF_3{\cdot}OEt_2$ at −20 °C.[42] After oxidative decomplexation with ferric nitrate, the cyclisation products **41a**,**b** (**a** : **b** = 95 : 5) were obtained in 97% overall yield from propargylic alcohols **38** and the major diastereoisomer (+)-**41a** purified by crystallisation from MeOH–H_2O. The absolute stereochemistry of (−)-**41a** and the *cis*-relationship of the methyl and ethynyl substituents were ascertained by X-ray crystallography (see below).

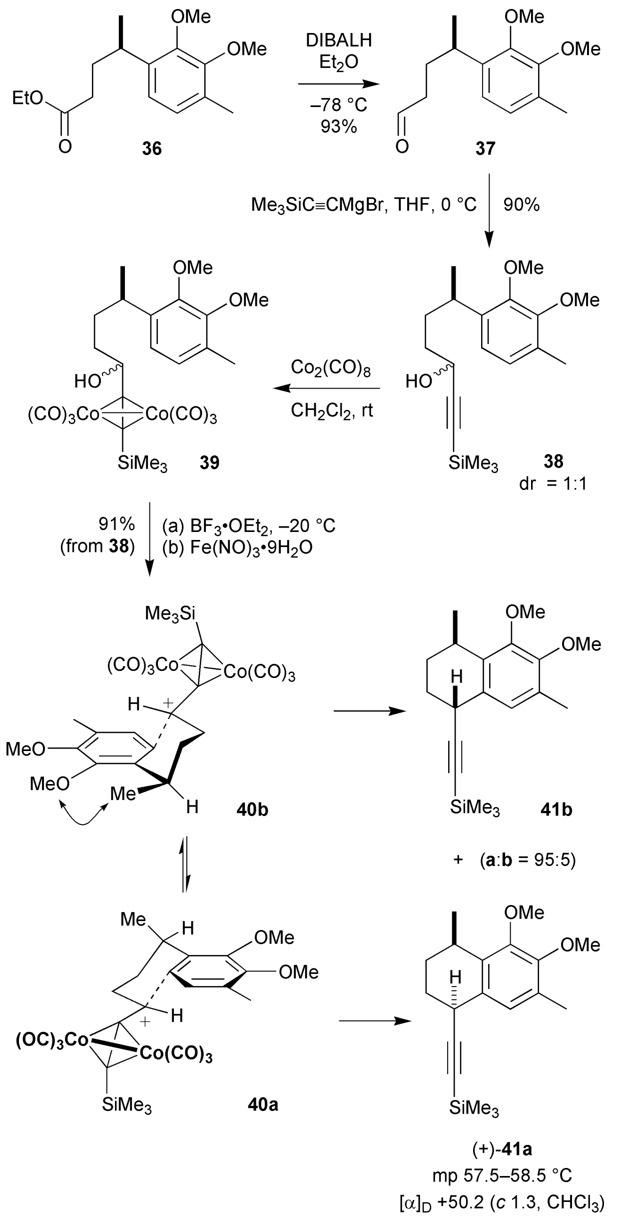
The stereoselectivity of the cyclisation can be rationalised in terms of two competing pathways involving propargylic cations **40a** and **40b**. Both cations have a chair conformation for the nascent ring and both place the bulky cobalt-complexed side chain in the equatorial position. However $A^{1,3}$-strain[43] engendered by a steric clash between the methyl substituent at C6 and the proximate methoxy group penalises cyclisation *via* cation **40b**.

Construction of ring C

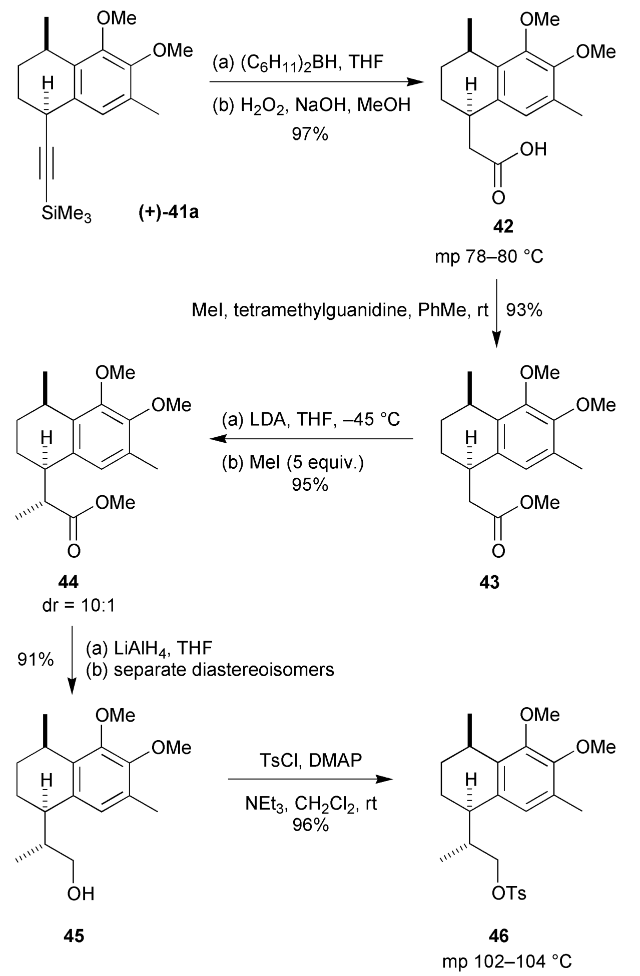
Before construction of ring C could begin in earnest, it was necessary to elaborate the ethynyl chain and install the stereogenic centre at C3 (Scheme 7). The sequence began with the hydroboration–oxidation of silylalkyne **41a** to release the latent acetic acid side chain in **42**. The yield was excellent (97%) and as a bonus, the product **42** was crystalline. Esterification of **42** with iodomethane using tetramethylguanidine as base returned the ester **43** (93%). Introduction of the C3 stereogenic centre was easily accomplished by alkylation of the lithium enolate of ester **43** with iodomethane. The yield (95%) and diastereoselectivity (10 : 1) of the alkylation were optimum when the reaction was conducted at −45 °C. The diastereoisomers of **44** were not

‖ The diastereoisomeric Mosher ester derivatives prepared from (±)-**36** gave singlets in the ^{19}F NMR spectrum at δ_F −72.0077 and −72.00332.

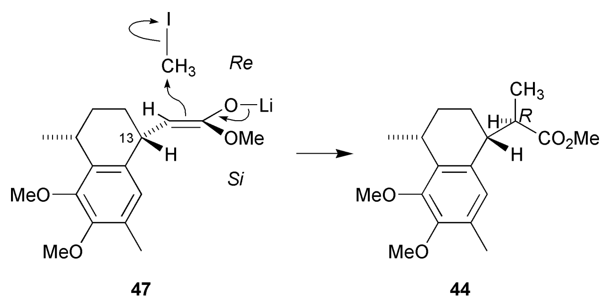
** We recently discovered that the *isopropyl* ester corresponding to the cationic η^3-allylmolybdenum complex **28a–d** gave an improved ratio (5 : 95) of adducts derived from reaction with arylcopper(I) reagent **32**.



Scheme 6



Scheme 7



Scheme 8

separable but the corresponding alcohols **45** derived by reduction with lithium aluminium hydride were separable by column chromatography. However, diastereoisomeric purity was best achieved at the final step in the sequence by simple crystallisation of the tosylate **46**. The overall yield for the 5-step conversion of silylalkyne **41a** to the tosylate **46** was 75%.

The good level of substrate control in the alkylation reaction can be rationalised using the model depicted in Scheme 8. The desired (*R*)-stereochemistry is a consequence of alkylation taking place selectively from the less hindered *Re*-face of the enolate **47** in which the C13–H bond resides in the plane of the enolate in order to minimise $A^{1,3}$-strain.

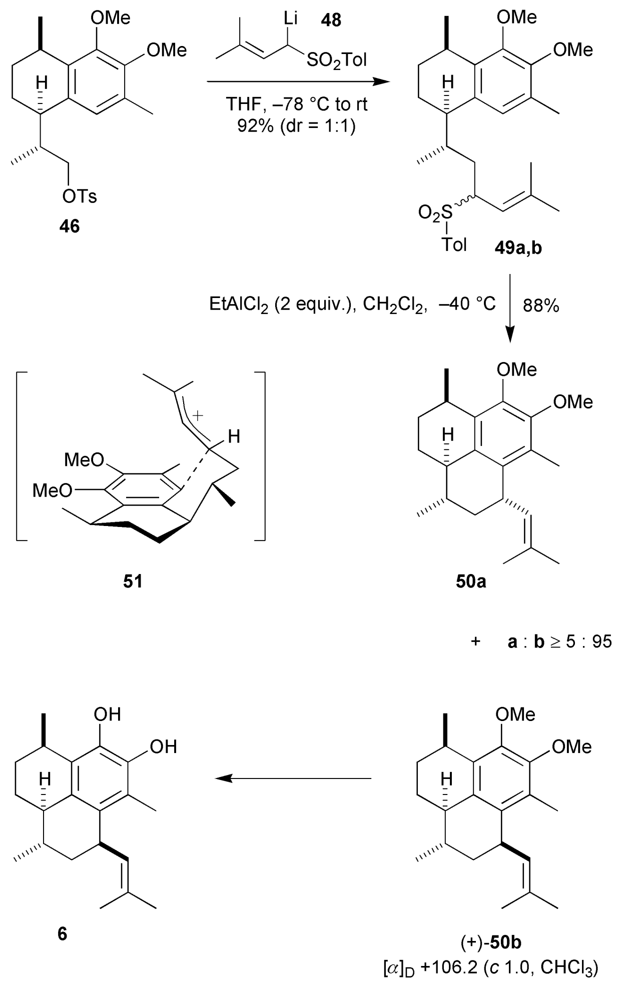
To complete the synthesis (Scheme 9), nucleophilic displacement of the tosylate **46** with 4 equiv. of the lithium derivative 3,3-dimethylallyl *p*-tolyl sulfone (**48**) gave a 92% yield of the alkylation product **49** as a 1 : 1 mixture of diastereoisomers. The lack of stereocontrol in the alkylation was of no practical consequence since treatment of the mixture with 2 equiv. of ethylaluminium dichloride at −40 °C resulted in rapid and clean cyclisation[44] to give the tricyclic aglycone dimethyl ethers **50a**,**b** in 88% yield as a mixture of diastereoisomers in favour of the desired (1*R*) stereochemistry (**a** : **b** = 5 : 95). The relative configuration of pure (+)-**50b** obtained by crystallisation from methanol was identical by a single crystal X-ray crystallographic analysis to that reported for pseudopterosin G–J aglycone.††

The stereochemistry of the final cyclisation can be rationalised by assuming that both diastereoisomeric sulfones converge to the same allylic cation **51**. Electrophilic attack of the allyl cation on the arene ring then occurs *via* a chair conformation which places the alkene substituent in an axial position in order to avoid $A^{1,3}$-strain with the aryl methyl group. Evidence that the cyclisation occurred under kinetic control was obtained by treating mixtures of **50a**,**b** enriched in **50a** with camphorsulfonic acid or ethylaluminium dichloride under the same conditions used for the cyclisation. In neither case was isomerisation to **50b** observed.

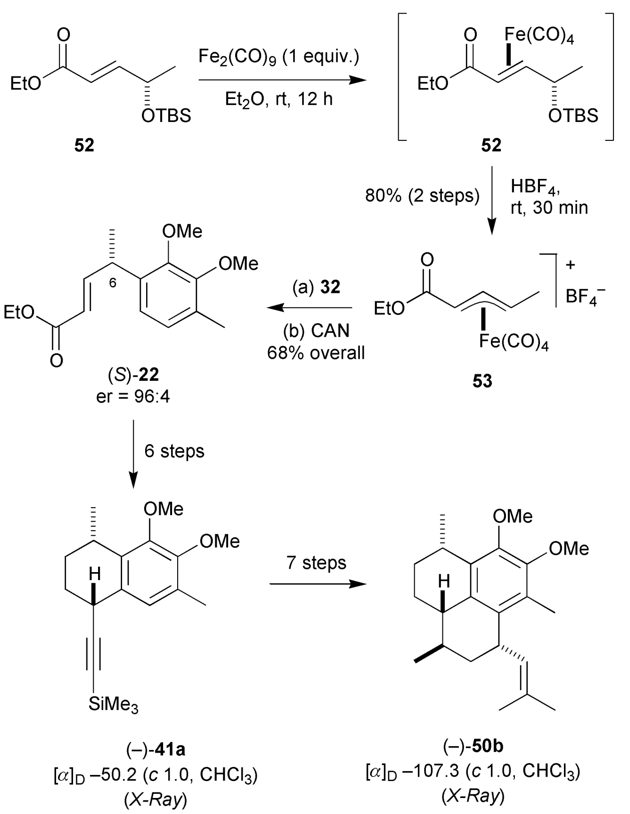
A comparison of π-allyl cationic complexes of molybdenum and iron

In order to gauge the value of the molybdenum complex **28**

†† The X-ray analysis was determined on the enantiomer, (−)-**50b**.[26] The enantiomeric relation between (−)-**50b** and (+)-**50b** was ascertained by optical rotation, mp and ^{1}H and ^{13}C NMR spectroscopy.



Scheme 9



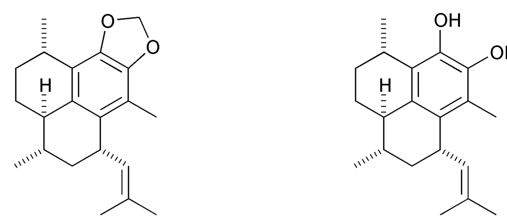
Scheme 10

in relation to its iron counterpart, we synthesised putative pseudopterosin G aglycone dimethyl ether using complex **53** which we prepared (Scheme 10) by a slight modification of the route described by Enders and co-workers.[27] The (*S*)-allylic TBS ether derivative **24** used in the molybdenum series described above was treated with 1 equiv. of diiron nonacarbonyl in ether to give an intermediate η^2-complex **52** which was treated with fluoroboric acid in Et_2O to afford the complex **53** as a yellow powder in 80% yield. Addition of iron complex **53** to a solution of arylcopper **32**‡‡ in THF gave (*S*)-**22** in 68% yield after oxidative decomplexation with CAN. Thus the yields of the two series are comparable (*cf.* 72% for the Mo series) as are the enantiomeric ratios but the iron series—devoid of the complication of central chirality at the metal—gave a single regioisomer whereas the Mo series gave a 1 : 6 mixture.

Ester (*S*)-**22** was converted to the crystalline silylalkyne (−)-**41a** whose absolute configuration (X-ray crystallography) established conclusively that the Fe and Mo routes were stereocomplementary. Thus, substitution of the (*S*)-allylic TBS ether **24** *via* the Mo cationic complex **28** occurred with overall inversion to produce (*R*)-**22** whereas the analogous chemistry on (*S*)-allylic TBS ether **24** *via* the Fe cationic complex **53** occurred with overall retention to produce (*S*)-**22**. Finally, an X-ray structure of the *enantiomer* of putative pseudopterosin G aglycone dimethyl ether [(−)-**50b**], derived from (−)-**41a** by the chemistry described above, proved the relative configuration of the 4 stereogenic centres.

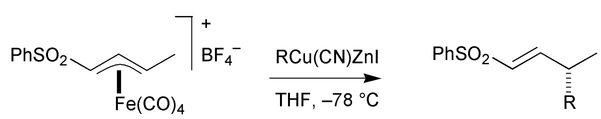
The correct stereochemistry of pseudopterosin G–J aglycone is revealed

The ^{1}H and ^{13}C NMR spectroscopic data for compound (−)-**50b** and those reported[2,4] for pseudopterosin G and its aglycone are very similar with the exception of the signals for carbons 3 and 4. Compound (−)-**50b** gives signals at δ 29.7 (C3) and 22.6 (C4) whereas the corresponding signals for pseudopterosin G appear at δ 34.2 and 27.6 and for the aglycone at δ 34.1 and 27.8 respectively. On the basis of these data, we suggested that the stereochemistry originally assigned to pseudopterosin G may require revision.[26] At the same time, Schmalz and co-workers[45–47] proved that the stereochemistry originally assigned to the closely related helioporin D[7] was also incorrect by total synthesis. Corey and co-workers[48] recently proved that the correct stereochemistry for helioporin E and pseudopterosin G–J aglycone is depicted by structures **54** and **55** respectively.



54 **55**

‡‡ Zinc cuprates add to the related (η^3-allyl)iron tetracarbonyl complex **56** to give the adducts **57** with excellent regio- and stereo-control after oxidative decomplexation.[41,51]



56 **57**

The arylzinc cuprate **21** [M = Cu(CN)ZnI] and the corresponding arylcopper(I) reagent **32** give comparable yields in the reaction with both the molybdenum complex **28a**–**d** and the iron complex **54** but **32** is easier to prepare.

Conclusions

The A⟶AB⟶ABC annulation strategy produced putative pseudopterosin G aglycone dimethyl ether in 16% overall yield for the longest linear sequence of 13 steps from commercial 2,3-dimethoxytoluene. A salient feature of the synthesis was the use of planar chiral η^3-allylmolybdenum cationic complex **28** bearing an electron withdrawing ester group to control the stereochemistry at C6. Such complexes are rare§§ and our discovery of convenient and mild conditions for the preparation of neutral η^3-allylmolybdenum precursors from allyl benzoates using $Mo(CO)_4(Py)_2$ opens a path to other functionalised η^3-allyl molybdenum cationic complexes of promising synthetic utility. Another noteworthy feature of our synthesis was the economy of means: all three bonds appended to the aromatic ring were created using allyl cations or their equivalents and the creation of the three stereogenic centres at C1, C3 and C13 was governed by the minimisation of $A^{1,3}$-strain. Moreover, once the stereogenic centre at C6 was created, the remaining three stereogenic centres were constructed by substrate controlled reactions.

Experimental

General aspects

^{1}H and ^{13}C NMR spectra were recorded in Fourier Transform mode at the field strength specified. All spectra were obtained in $CDCl_3$ or C_6D_6 solution in 5 mm diameter tubes, and the chemical shift in ppm is quoted relative to the residual signals of chloroform (δ_H 7.27, δ_C 77.2) or C_6H_6 (δ_H 7.10, δ_C 126.7) as the internal standard unless otherwise specified. Multiplicities in the ^{1}H NMR spectra are described as: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet and br = broad. Coupling constants (*J*) are reported in Hz. Numbers in parenthesis following the chemical shift in the ^{13}C NMR spectra refer to the number of protons attached to that carbon as revealed by the Distortionless Enhancement by Phase Transfer (DEPT) spectral editing technique, with secondary pulses at 90° and 135°. Signal assignments were based on COSY, HMQC and HMBC correlations. Pseudopterosin numbering (structure **9**, Scheme 2) was used throughout in assigning NMR signals. 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%). Mass spectra were recorded on samples judged to be ≥95% pure by ^{1}H and ^{13}C NMR spectroscopy unless otherwise stated. Optical rotations were measured on an Optical Activity AA-100 instrument at room temperature and are given in 10^{-1} deg cm^2 g^{-1}.

Ethyl (*E*,*S*)-4-benzoyloxypent-2-enoate (26)

To a solution of hydroxy ester **25**[36] (1.50 g, 10.40 mmol) in CH_2Cl_2, at 0 °C, were added successively DMAP (60 mg, 0.52 mmol), triethylamine (2.2 ml, 15.80 mmol), and finally benzoyl chloride (1.3 ml, 11.44 mmol). The reaction mixture was allowed to warm to rt and stirred for 5 h whereupon it was diluted with CH_2Cl_2 (30 ml) and shaken with water (20 ml). The resulting mixture was separated and the aqueous layer extracted with Et_2O (2 × 15 ml). The combined organic layers were washed with brine (20 ml), dried over $MgSO_4$, and concentrated *in vacuo*. The pale yellow residue was purified by column chromatography (SiO_2, hexanes–Et_2O, 4 : 1) to afford the diester **26** (2.48 g, 9.99 mmol, 96%) as a colourless oil: $[a]_D^{21}$ = +61.7 (*c*, 1.5 in $CHCl_3$); ν_{max} film/cm^{-1} 2982 s, 1715 m, 1662 s, 1601 s, 1451 s, 1268 m, 1178 s, 1111 m, 976 s, 869 s, 711 s; δ_H (400 MHz, $CDCl_3$): 8.08 (2H, dd, *J* 7.6, 1.4), 7.58 (1H, dt, *J* 7.7, 1.4), 7.47 (2H, ddd *J* 7.6, 7.6, 1.6), 7.00 (1H, dd, *J* 15.8, 4.9, C3H), 6.05 (1H, dd, *J* 15.8, 1.6, C2H), 5.76 (1H, ddq, *J* 6.6, 4.9, 1.6, C4H), 4.20 (2H, q, *J* 7.1, C*H*$_2$CH$_3$), 1.50 (3H, d, *J* 6.7, C5H$_3$), 1.34 (3H, t, *J* 7.1, C*H*$_3$CH$_2$); δ_C (100 MHz, $CDCl_3$): 166.04 (0, C1), 165.43 (0, C6), 146.34 (1, C2), 133.22 (1, phenyl), 130.00 (0, C7), 129.68 (1, 2C, phenyl), 128.46 (1, 2C, phenyl), 121.12 (1, C3), 69.41 (1, C4), 60.60 (2, OCH$_2$CH$_3$), 19.78 (3, OCH$_2$CH$_3$), 14.24 (3, C5); *m*/*z* (EI) 248 ($M^{+\bullet}$, 5%), 127 ($M^{+\bullet}$ − O, 20), 105 ($C_6H_5CO^+$, 100); Found $M^{+\bullet}$, 248.1050; $C_{14}H_{16}O_4$ requires *M*, 248.1049.

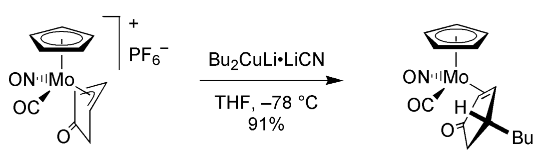
syn,*syn*-Dicarbonyl-η^5-cyclopentadienyl-[2,3,4-η-(2*R*,3*S*,4*S*)-1-ethoxy-1-oxopent-2-enyl]molybdenum (27a,b)

Molybdenum hexacarbonyl (0.81 g, 3.0 mmol) was placed under nitrogen in a two-necked flask equipped with condenser, and THF (35 ml) was added. The molybdenum hexacarbonyl was dissolved by stirring and refluxing (oil bath, ~110 °C) and after 30 min, pyridine (0.5 ml, 6.0 mmol) was added to the bright yellow solution. The reaction mixture was refluxed for 12 h, during which an intense orange–red solution developed, and neat benzoate (0.71 g, 0.65 ml, 2.85 mmol) was added dropwise to the refluxing reaction mixture. After 72 h, the reaction mixture was cooled to rt, and a solution of LiCp [freshly prepared with cyclopentadiene (0.28 ml, 3.3 mmol) and *n*-BuLi (2.32 M in hexanes, 1.36 ml, 3.15 mmol)] in THF (4 ml) was added, and allowed to stir for 1 h. The resulting golden mixture was partially concentrated *in vacuo*, and then chromatographed under nitrogen using degassed eluents (alumina, hexanes–Et_2O, 50 : 50⟶0 : 100) to afford the molybdenum complex (0.86 g, 2.5 mmol, 88%) as an air/moisture sensitive orange–yellow oil: ν_{max} film/cm^{-1} 3110 s, 2980 s, 1956 s, 1877 s, 1695 s, 1511 s, 1455 m, 1402 s, 1252 s, 1152 s, 1029 m, 813 s, 764 s; δ_{Mo} (13.043 MHz, C_6D_6): −1576 (**27a**, 77%, *exo*,*syn*,*syn*), −1388 (**27b**, 13%, *endosyn*,*syn*), and two minor products at −1517 (8%, possibly the ,*exo*,*anti*,*syn* isomer) and −1571 (2%, possibly the *endo*,*anti*,*syn* isomer); δ_H (400 MHz, C_6D_6, data only for **27a**): 4.81 (5H, s, Cp), 4.69 (1H, dd, *J* 9.3, 9.3, C3H), 3.96–4.14 (2H, m, C*H*$_2$CH$_3$), 1.63–1.71 (1H, m, C3H), 1.60 (1H, d, *J* 9.3, C2H), 1.45 (3H, d, *J* 6.3, C5H$_3$), 1.08 (3H, d, *J* 7.1, C*H*$_3$CH$_2$); δ_C (100 MHz, C_6D_6, data only for *exo*,*syn*,*syn*-isomer): 240.03 (0, CO), 236.91 (0, CO), 174.81 (0, C1), 94.03 (5C, d, Cp), 74.03 (1, C4), 62.51 (1, C3), 60.25 (2 CH$_2$CH$_3$), 42.87 (1, C2), 20.78 (3, C5), 14.58 (3, CH$_3$CH$_2$); *m*/*z* (EI) 346 [$M^{+\bullet}$ (^{98}Mo), 10%], 318 ($M^{+\bullet}$ − CO, 10%), 290 ($M^{+\bullet}$ − 2CO, 13%); Found $M^{+\bullet}$, 346.0106; $C_{14}H_{16}{}^{98}MoO_4$ requires *M*, 346.0106.

1-Iodo-2,3-dimethoxy-4-methylbenzene (30)

To a solution of 2,3-dimethoxytoluene **29** (5.26 g, 34.6 mmol) and TMEDA (1.2 ml, 8 mmol) in hexane (60 ml), at rt, was added dropwise *t*-BuLi (1.75 M in pentane, 20.7 ml, 36 mmol). The resulting cloudy yellow solution was stirred at rt for 8 h and then cooled to 0 °C whereupon 1,2-diiodoethane (10.23 g, 36 mmol) was added portionwise. The resulting slurry was allowed to warm to rt over 2 h, and then diluted with hexanes (50 ml) and washed with HCl (2 M, 20 ml), sat. aq. $NaHCO_3$ solution (20 ml), dried over $MgSO_4$, and concentrated *in vacuo*. The yellow residue was purified by column chromatography (SiO_2, hexanes–Et_2O 98 : 2) to give the iodoarene **30** (7.18 g, 25.8 mmol, 75%) as a colourless oil: ν_{max} film/cm^{-1} 2937 s, 1581 m, 1477 s, 1407 s, 1287 s, 1143 s, 1063 s, 1013 s, 928 m, 854 s, 809 s; δ_H (400 MHz, $CDCl_3$): 7.38 (1H, d, *J* 8.1, C5H), 6.69 (1H, d,

§§ Liebeskind and co-workers[52] reported the preparation of complex **58** and its regio- and stereo-selective reaction with cyanocuprates.



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J 8.1, C6H), 3.86 (3H, s, OMe), 3.84 (3H, s, OMe), 2.24 (3H, s, C7H$_3$); δ_C (100 MHz, CDCl$_3$): 152.97, 151.78 (0, C2, C3), 133.41, 127.90 (1, C5, C6), 126.33 (0, C4), 88.96 (0, C1), 60.56, 60.39 (3, 2 × OMe), 15.83 (3, C7).

Ethyl (*R*)-4-(2,3-dimethoxy-4-methylphenyl)pentanoate (36)

To a solution of 1-iodo-2,3-dimethoxy-4-methylbenzene **30** (2.46 g, 8.84 mmol) in THF (40 ml) at −78 °C, was added dropwise BuLi (2.32 M in hexane, 4.2 ml, 9.72 mmol). After 15 min, to the resulting pale yellow solution was added dropwise a solution of CuBr·SMe$_2$ in diisopropyl sulfide (2 ml) and THF (2 ml) maintaining the temperature below −75 °C. The mixture was stirred at −78 °C for 45 min before cooling to −90 °C and addition of a solution of cationic molybdenum complex **28a**–**d** [prepared freshly from neutral complex **27a**,**b** (2.34 g, 6.80 mmol) and NOBF$_4$ (0.83 g, 7.14 mmol) in acetonitrile (5 ml)]. The resulting brown reaction mixture was stirred at −78 °C for 1 h before addition of NH$_4$OH (20 ml) and saturated aqueous NH$_4$Cl solution (20 ml). After warming to rt the phases were separated and the aqueous layer was extracted with Et$_2$O (3 × 15 ml). The combined organic layers were washed with brine (20 ml), dried over MgSO$_4$ and concentrated *in vacuo*. The orange coloured residue was dissolved in THF (20 ml) and Et$_2$O (5 ml) and at 0 °C, an aqueous solution of ceric ammonium nitrate (1 M, 20 ml) was added. The resulting brown mixture was stirred at rt for 30 min, when TLC showed that decomplexation was complete, whereupon the mixture was diluted with Et$_2$O (25 ml) and washed with water (30 ml). The aqueous layer was extracted with Et$_2$O (3 × 10 ml) and the combined extracts were washed with brine (20 ml), dried over MgSO$_4$ and concentrated *in vacuo*. The red residue was purified by column chromatography (SiO$_2$, hexanes–Et$_2$O 90 : 10) to afford an inseparable mixture of regioisomers **35** and (*R*)-**22** (1 : 6) (1.37 g, 4.92 mmol, 72%) as a colourless oil.

To a mixture of esters **35** and (*R*)-**22** (1.52 g, 5.45 mmol) in methanol (30 ml), at 0 °C was added magnesium turnings (1.34 g, 55 mmol). The reaction mixture was allowed to stir at 0 °C for 7 h and then diluted with hexanes (40 ml) and Et$_2$O (40 ml), and then filtered through Celite. The filtrate was washed with HCl (2 M, 15 ml), sat. aq. NaHCO$_3$ solution (10 ml), dried over MgSO$_4$, and concentrated *in vacuo*. The yellow residue was purified by column chromatography (SiO$_2$, hexanes–Et$_2$O 85 : 15) to give methyl ester **36** (1.06 g, 4.0 mmol, 87%) as a colourless oil and the unchanged regioisomer **35** (0.12 g, 0.43 mmol, *cis* : *trans* = 1 : 5). Data were collected for **36**: ν_{max} film/cm^{-1} 2967 s, 1716 s, 1464 s, 1411 s, 1280 s, 1076 s, 1023 s; δ_H (400 MHz, CDCl$_3$): 6.87 (1H, d, *J* 8.0, C11H), 6.81 (1H, d, *J* 8.0, C10H), 3.83 (3H, s, OMe), 3.82 (3H, s, OMe), 3.63 (3H, s, CO$_2$Me), 3.14–3.16 (1H, m, C6H), 2.19–2.27 (2H, m, C4H$_2$), 2.24 (3H, s, C20H$_3$), 1.86–1.92 (2H, m, C5H$_2$), 1.22 (3H, d, *J* 7.0, C19H$_3$); δ_C (100 MHz, CDCl$_3$): 174.39 (0, C13), 151.49, 151.06 (0, C7, C8), 137.94, 130.01 (0, C9, C12), 125.93, 121.53 (1, C10, C11), 60.80, 60.06 (3, 2 × OMe), 51.60 (3, CO$_2$*C*H$_3$), 32.73, 32.64 (2, C4, C5), 31.73 (1, C6), 22.01 (3, C19), 15.82 (3, C20); *m*/*z* (EI) 266 (M$^{+\bullet}$, 10%), 235 (18), 193 (17), 179 (100), 164 (27), 91 (15), 74 (28), 59 (40); Found: C, 67.68; H, 8.16%. $C_{15}H_{22}O_4$ (*M* = 266) requires C, 67.64; H, 8.33.

(*R*)-4-(2,3-Dimethoxy-4-methylphenyl)pentanal (37)

To a solution of methyl ester **36** (2.57 g, 9.7 mmol) in Et$_2$O (30 ml), at −78 °C was added DIBAL-H (neat, 1.9 ml, 10.6 mmol) dropwise. The reaction mixture was allowed to stir at −78 °C for 30 min and then quenched with sat. aq. Na$_2$SO$_4$ solution (20 ml), allowed to warm to rt and then filtered through Celite. The filtrate was successively washed with water (2 × 20 ml), sat. aq. NaHCO$_3$ solution (10 ml), dried over MgSO$_4$, and concentrated *in vacuo*. The yellow residue was purified by column chromatography (SiO$_2$, hexanes–Et$_2$O 85 : 15) to afford the desired aldehyde **37** (1.93 g, 8.2 mmol, 85%) as a colourless oil: $[\alpha]_D^{18}$ −7.2 (*c* 1.2, CHCl$_3$); ν_{max} film/cm^{-1} 2967 s, 1732 s, 1464 s, 1411 s, 1285 s, 1222 s, 1075 s, 1033 s; δ_H (400 MHz, CDCl$_3$): 9.69 (1H, t, *J* 1.6, C13H), 6.88 (1H, d, *J* 7.9, C11H), 6.81 (1H, d, *J* 7.9, C10H), 3.83 (3H, s, OMe), 3.82 (3H, s, OMe), 3.11–3.20 (1H, m, C6H), 2.30–2.39 (2H, m, C4H$_2$), 2.25 (3H, s, C20H$_3$), 1.85–1.94 (2H, m, C5H$_2$), 1.24 (3H, d, *J* 7.0, C19H$_3$); δ_C (100 MHz, CDCl$_3$): 202.77 (1, C13), 151.54, 151.07 (0, C7, C8), 137.73, 130.21 (0, C9, C12), 126.00, 121.49 (1, C10, C11), 60.83, 60.08 (3, 2 × OMe), 42.48 (2, C4), 31.67 (1, C6), 30.05 (2, C5), 21.99 (3, C19), 15.84 (3, C20); *m*/*z* (EI) 236 (M$^{+\bullet}$, 20%), 192 (25), 179 (100), 164 (35), 149 (12), 91 (14); Found: C, 70.41; H, 8.67%. $C_{14}H_{20}O_3$ (*M* = 236) requires C, 71.16; H, 8.53.

(3*RS*,6*R*)-6-(2,3-Dimethoxy-4-methylphenyl)-1-trimethylsilyl-hept-1-yn-3-ol (38)

To a solution of trimethylsilylacetylene (1.70 ml, 12.0 mmol) in THF (30 ml) at 0 °C was added dropwise EtMgBr (1.40 M in THF, 7.4 ml, 10.4 mmol). The resulting pale yellow solution was slowly warmed to rt within 1 h, and then cooled to 0 °C before adding a solution of aldehyde **37** (1.90 g, 8.0 mmol) in THF (15 ml). After 20 min, the reaction mixture was quenched with water (15 ml). The resulting layers were separated, and the aqueous layer was extracted with Et$_2$O (3 × 20 ml). The combined organic layers were washed with brine (30 ml), dried over MgSO$_4$, and concentrated *in vacuo*. The yellow residue was purified by column chromatography (SiO$_2$, hexanes–Et$_2$O 75 : 25) to afford the desired propargylic alcohol **38** (2.42 g, 7.2 mmol, 90%) as a mixture of diastereoisomers (1 : 1): ν_{max} film/cm^{-1} 3450 s, 2967 s, 2168 s, 1464 s, 1412 s, 1280 s, 1222 s, 1065 s, 1023 s, 849 s; δ_H (400 MHz, CDCl$_3$): 6.88 (1H, d, *J* 8.0, C11H), 6.83 (1H, d, *J* 8.0, C10H), 4.31–4.37 (1H, m, C13H), 3.85 (3H, s, OMe), 3.83 (3H, s, OMe), 3.13–3.20 (1H, m, C6H), 2.25 (3H, s, C20H$_3$), 1.94 (1H, d, *J* 5.6, OH), 1.54–1.76 (4H, m, C4H$_2$, C5H$_2$), 1.23 (0.5 × 3H, d, *J* 6.9, C19H$_3$), 1.22 (0.5 × 3H, d, *J* 6.9, C19H$_3$), 0.17 (9H, s, SiMe$_3$); δ_C (100 MHz, CDCl$_3$): 151.45, 150.92 (0, C7, C8), 138.74, 129.80 (0, C9, C12), 125.92, 121.52 (1, C10, C11), 107.07 (0, C2), 89.40 (0, C3), 63.13, 63.03 (1, C13), 60.88, 60.08 (3, 2 × OMe), 36.18, 36.05 (2, C5), 33.40, 33.10 (2, C4), 31.77, 31.74 (1, C6), 22.30, 22.24 (3, C19), 15.82 (3, C20), 0.06 (3, SiMe$_3$); *m*/*z* (EI) 334 (M$^{+\bullet}$, 0.2%), 316 (25), 194 (100), 179 (95), 152 (30), 73 (25); Found: C, 67.98; H, 9.11%. $C_{19}H_{30}O_3Si$ (*M* = 334) requires C, 68.22; H, 9.04.

(5*S*,8*R*)-1,2-Dimethoxy-3,8-dimethyl-5-(2-trimethylsilyl-ethynyl)-5,6,7,8-tetrahydronaphthalene [(+)-41a]

To a solution of alkynols **38** (3.05 g, 9.1 mmol) in CH$_2$Cl$_2$ (70 ml), at rt was added dicobalt octacarbonyl (3.43 g, 10.0 mmol) in one portion. The mixture was allowed to stir for 1 h before cooling to −20 °C, and BF$_3$·OEt$_2$ (2.3 ml, 18.2 mmol) was added dropwise. The deep red reaction mixture was allowed to stir at −20 °C for 3 h, and then quenched with a sat. aq. NaHCO$_3$ solution (25 ml). The resulting layers were separated, and the aqueous layer was extracted with hexanes and Et$_2$O (1 : 1, 3 × 40 ml). The combined organic layers were dried over MgSO$_4$ and concentrated *in vacuo*. The dark red–brown residue was purified by column chromatography (SiO$_2$, hexanes–Et$_2$O 95 : 5) to give the diastereoisomeric dicobalt hexacarbonyl complexes of **41a**,**b** (5.33 g, 8.9 mmol, 97%) as a dark red–brown solid. The diastereoisomeric ratio was measured after decomplexation; ν_{max} film/cm^{-1} 2958 s, 2938 s, 2084 s, 2010 s, 1566 s, 1480 s, 1448 s, 1406 s, 1318 s, 1262 s, 1250 s, 1072 s, 1026 s, 840 s, 758 s; δ_H (400 MHz, CDCl$_3$): 7.03 (1H, s, C10H), 4.18–4.22 (1H, m, C13H), 3.88 (3H, s, OMe), 3.76 (3H, s, OMe), 3.19 (1H, m, C6H), 2.21 (3H, s, C20H$_3$), 2.05 (2H, m, C4H$_2$), 1.84 (2H, m, C5H$_2$), 1.31 (3H, d, *J* 6.5, C19H$_3$), 0.41 (9H, s, SiMe$_3$); δ_C (100 MHz, CDCl$_3$): 200.53 (6 × CO), 150.65, 150.02 (0, C7, C8), 134.67, 133.94, 129.39 (0, C9, C11, C12), 126.52 (1, C10), 120.73 (0, C2), 81.13 (0, C3), 60.47, 60.02 (3, 2 × OMe), 41.53

(2, C4), 29.67, 29.31 (1, C6, C13), 27.80 (2, C5), 21.07 (3, C19), 15.61 (3, C20), 1.49 (3, $SiMe_3$); *m*/*z* (EI) 384 (30), 360 (55), 314 (27), 298 (30), 247 (36), 229 (34).

To a solution of dicobalt hexacarbonyl complexes of **41a**,**b** (3.80 g, 6.3 mmol) in methanol (100 ml), at 0 °C was added $Fe(NO_3)_3 \cdot 9H_2O$ (25.45 g, 63.0 mmol). The reaction mixture was allowed to stir for 3 h at rt and then diluted with a mixture of hexanes and Et_2O (4 : 1, 200 ml), and washed with a sat. aq. $NaHCO_3$ solution (100 ml). The layers were separated, and the aqueous layer was extracted with hexanes and Et_2O (4 : 1, 2 × 30 ml). The combined organic layers were dried over $MgSO_4$, stirred over activated carbon (Norit SA3), and concentrated *in vacuo*. The pale orange residue was purified by column chromatography (SiO_2, hexanes–Et_2O 95 : 5) to afford the silylalkyne **41a**,**b** (1.87 g, 5.9 mmol, 94%, dr = 95 : 5) as a colourless oil. The desired silylalkyne derivative **41a** (1.75 g, 91%, dr ≥ 99 : 1) was obtained as colourless crystals after crystallisation from MeOH–H_2O: mp 57.5–58.5 °C; $[a]_D^{19}$ +50.2 (*c* 1.3, $CHCl_3$); ν_{max} film/cm^{-1} 2954 s, 2171 s, 2019 m, 1477 s, 1405 s, 1316 s, 1250 s, 1068 s, 1027 s, 912 m, 843 s, 760 m, 733 m, 644 m, 464 m; δ_H (400 MHz, $CDCl_3$): 7.16 (1H, s, C10H), 3.89 (3H, s, OMe), 3.81 (3H, s, OMe), 3.68 (1H, dd, *J* 5.8, 11.0, C13H), 3.10–3.18 (1H, m, C6H), 2.26 (3H, s, $C20H_3$), 2.195–2.07 (2H, m, $C4H_2$), 1.80–1.73 (2H, m, $C5H_2$), 1.26 (3H, d, *J* 7.0, $C19H_3$), 0.20 (9H, s, $SiMe_3$); δ_C (100 MHz, $CDCl_3$): 150.78, 149.95 (0, C7, C8), 133.35, 131.04, 129.87 (0, C9, C11, C12), 125.72 (1, C10), 110.26 (0, C2), 85.18 (0, C3), 60.46, 59.92 (3, 2 × OMe), 33.12 (1, C13), 29.70 (2, C4), 27.47 (1, C6), 25.86 (2, C5), 22.31 (3, C19), 15.91 (3, C20), 0.36 (3, $SiMe_3$); *m*/*z* (EI) 316 ($M^{+\bullet}$, 100%), 274 (70), 259 (13), 149 (12), 143 (13), 73 (18); Found: C, 72.02; H, 9.11%. $C_{19}H_{28}O_2Si$ (*M* = 316) requires C, 72.10; H, 8.92.

2-[(5*S*,8*R*)-(1,2-Dimethoxy-3,8-dimethyl-5,6,7,8-tetrahydro-5-naphthyl)]ethanoic acid (42)

A solution of dicyclohexylborane was freshly prepared from cyclohexene (0.9 ml, 9.1 mmol) and $BH_3 \cdot THF$ (1.0 M, 4.2 ml, 4.2 mmol) in THF at 0 °C for 2 h. A solution of silylalkyne **41a** (0.67 g, 2.10 mmol) in THF (10 ml) was added dropwise to the resulting white suspension over 20 min. The reaction mixture was allowed to warm to rt and stirred for 1 h to form a homogeneous solution. The clear reaction mixture was diluted with methanol (4 ml), then oxidised by dropwise addition of NaOH (3 M, 3 ml) followed by H_2O_2 (30%, 4 ml) keeping the temperature between 30 °C and 50 °C (the oxidation was exothermic and caused a strong evolution of H_2). After stirring for 30 min at rt, NaOH (3 M, 3 ml) was added and the layers were separated. The cyclohexanol by-product was removed with Et_2O (2 × 30 ml), and the aqueous layer acidified with HCl (conc., 2 ml) and extracted with Et_2O (3 × 30 ml). The combined organic layers were dried over Na_2SO_4, and concentrated *in vacuo*. The yellow residue was purified by column chromatography (SiO_2, hexanes–Et_2O 60 : 40) to afford the carboxylic acid **42** (0.57 g, 2.06 mmol, 97%) as a colourless oil which crystallised on storage in the refrigerator: mp 78–80 °C; $[a]_D^{18}$ +47.9 (*c* 1.4, $CHCl_3$); ν_{max} film/cm^{-1} 2897 s, 1721 s, 1496 s, 1412 s, 1307 s, 1247 m, 1073 s, 1038 m, 923 s, 754 s; δ_H (400 MHz, $CDCl_3$): 11.05 (1H, br s, CO_2H), 6.81 (1H, s, C10H), 3.91 (3H, s, OMe), 3.84 (3H, s, OMe), 3.26–3.16 (2H, m, H6, C13H), 3.01 (1H, dd, *J* 4.3, 15.4, C3H), 2.50 (1H, dd, *J* 9.7, 15.3, C3H), 2.25 (3H, s, $C20H_3$), 1.99–1.94 (1H, m, C4H or C5H), 1.88–1.69 (3H, m, C4H, C5H), 1.28 (3H, d, *J* 6.9, $C19H_3$); δ_C (100 MHz, $CDCl_3$): 179.54 (0, C2), 150.91, 149.45 (0, C7, C8), 134.80, 134.08 (0, C11, C12), 129.67 (0, C9), 124.31 (1, C10), 60.38, 59.88 (3, 2 × OMe), 42.01 (2, C3), 34.80 (1, C13), 29.14 (2, C4), 27.63 (1, C6), 24.84 (2, C5), 22.11 (3, C19), 15.97 (3, C20); *m*/*z* (EI) 278 ($M^{+\bullet}$, 60%), 263 (10), 233 (20), 219 (100), 203 (35), 188 (17), 172 (7); Found: C, 69.01; H, 8.11%. $C_{16}H_{22}O_4$ (*M* = 278) requires C, 69.04; H, 7.97.

Methyl 2-[(5*S*,8*R*)-(1,2-dimethoxy-3,8-dimethyl-5,6,7,8-tetrahydro-5-naphthyl)]ethanoate (43)

To a solution of the carboxylic acid **42** (0.41 g, 1.5 mmol) in toluene (7 ml) at rt was added dropwise *N*,*N*,*N*′,*N*′-tetramethylguanidine (0.37 ml, 3.0 mmol). After 45 min, methyl iodide (0.28 ml, 4.5 mmol) was added and the mixture was allowed to stir at rt for 2.5 h. The resulting yellow mixture was diluted with Et_2O (20 ml) and washed with HCl (2 M, 10 ml), sat. aq. $NaHCO_3$ solution (10 ml), dried over $MgSO_4$ and concentrated *in vacuo*. The pale yellow residue was purified by column chromatography (SiO_2, hexanes–Et_2O 90 : 10) to afford methyl ester **43** (0.41 g, 1.4 mmol, 93%) as a colourless oil: $[a]_D^{21}$ +44.0 (*c* 1.1, $CHCl_3$); ν_{max} film/cm^{-1} 2937 s, 1751 s, 1497 s, 1452 s, 1417 s, 1337 s, 1242 s, 1173 s, 1078 s, 1048 s, 923 m, 873 m; δ_H (400 MHz, $CDCl_3$): 6.76 (1H, s, C10H), 3.89 (3H, s, OMe), 3.81 (3H, s, OMe), 3.73 (3H, s, CO_2Me), 3.22–3.14 (2H, m, C6H, C13H), 2.92 (1H, dd, *J* 4.5, 15.1, C3H), 2.44 (1H, dd, *J* 9.8, 15.1, C3H), 2.22 (3H, s, $C20H_3$), 1.89–1.76 (2H, m, $C4H_2$ or $C5H_2$), 1.71–1.61 (2H, m, $C4H_2$ or $C5H_2$), 1.25 (3H, d, *J* 6.9, H19); δ_C (100 MHz, $CDCl_3$): 173.52 (0, CO_2), 150.88, 149.38 (0, C7, C8), 134.73, 134.34 (0, C11, C12), 129.55 (0, C9), 124.31 (1, C10), 60.32, 59.83 (3, 2 × OMe), 51.68 (3, CO_2CH_3), 41.97 (2, C3), 34.97 (1, C13), 29.13 (2, C4), 27.63 (1, C6), 24.87 (2, C5), 22.08 (3, C19), 15.94 (3, C20); *m*/*z* (EI) 292 ($M^{+\bullet}$, 60%), 232 (7), 219 (100), 203 (30), 188 (15), 172 (7); Found: C, 69.73; H, 8.31%. $C_{17}H_{24}O_4$ (*M* = 292) requires C, 69.84; H, 8.27.

Methyl (*R*)-2-[(5*S*,8*R*)-(1,2-dimethoxy-3,8-dimethyl-5,6,7,8-tetrahydro-5-naphthyl)]propanoate (44)

To a solution of diisopropylamine (0.28 ml, 2.0 mmol) in THF (10 ml) at 0 °C, was added dropwise BuLi (2.32 M in hexane, 0.75 ml, 1.7 mmol). After 30 min, the reaction mixture was cooled to −45 °C before addition of a solution of methyl ester **43** (0.39 g, 1.3 mmol) in THF (2.5 ml) dropwise. The resulting pale yellow solution was maintained at −45 °C for 45 min and methyl iodide (0.42 ml, 6.7 mmol) was added dropwise. After a further 1.5 h at −45 °C, the reaction mixture was quenched with water (5 ml) and the resulting layers were separated. The aqueous layer was extracted with Et_2O (3 × 20 ml) and the combined organic layers were washed with brine (10 ml), dried over $MgSO_4$, and concentrated *in vacuo*. The pale yellow residue was purified by column chromatography (SiO_2, hexanes–Et_2O 10 : 1) to give methyl ester **44** (0.39 g, 6.7 mmol, 95%, dr = 10 : 1) as a colourless oil: $[a]_D^{21}$ +31.6 (*c* 1.3, $CHCl_3$); ν_{max} film/cm^{-1} 2947 s, 1751 s, 1492 s, 1417 s, 1332 s, 1252 s, 1208 s, 1078 s, 923 m, 749 m; δ_H (400 MHz, $CDCl_3$): 6.76 (1H, s, C10H), 3.88 (3H, s, OMe), 3.81 (3H, s, OMe), 3.72 (3H, s, CO_2Me), 3.32–3.13 (3H, m, C3H, C6H, C13H), 2.22 (3H, s, $C20H_3$), 1.79–1.67 (4H, m, $C4H_2$, $C5H_2$), 1.21 (3H, d, *J* 6.9, $C19H_3$), 0.96 (3H, d, *J* 7.0, $C18H_3$); δ_C (100 MHz, $CDCl_3$): 176.38 (0, CO_2), 150.64, 149.12 (0, C7, C8), 135.64, 132.90 (0, C11, C12), 129.45 (0, C9), 124.03 (1, C10), 60.33, 59.83 (3, 2 × OMe), 51.74 (3, CO_2Me), 42.86 (1, C3), 39.78 (1, C13), 28.87 (2, C4), 27.27 (1, C6), 21.79 (3, C19), 18.66 (2, C5), 16.00 (3, C20), 10.66 (3, C18); *m*/*z* (EI) 306 ($M^{+\bullet}$, 15%), 233 (5), 219 (100), 188 (10), 173 (5); Found: C, 70.42; H, 8.58%. $C_{18}H_{26}O_4$ (*M* = 306) requires C, 70.56; H, 8.55.

Signals for the (2*S*)-epimer which were clearly distinguished: δ_H (400 MHz, $CDCl_3$): 6.67 (1H, s, C10H), 3.87 (3H, s, OMe), 3.80 (3H, s, OMe), 3.63 (3H, s, CO_2Me), 1.21 (3H, d, *J* 6.9, $C19H_3$), 0.96 (3H, d, *J* 7.0, $C18H_3$); δ_C (100 MHz, $CDCl_3$): 176.51 (0, CO_2), 150.95, 149.41 (0, C7, C8), 134.80, 133.51 (0, C11, C12), 128.78 (0, C9), 125.71 (1, C10), 60.25, 59.83 (3, 2 × OMe), 51.54 (3, CO_2Me), 43.50 (1, C3), 41.34 (1, C13), 28.70 (2, C4), 27.52 (1, C6), 23.20 (3, C19), 22.63 (2, C5), 15.13 (3, C20), 10.66 (3, C18).

(5*S*,8*R*)-1,2-Dimethoxy-3,8-dimethyl-5-[(2*R*)-(1-methyl-2-hydroxyethyl)]-5,6,7,8-tetrahydronaphthalene (45)

To a suspension of $LiAlH_4$ (35 mg, 0.9 mmol) in THF (7 ml) at 0 °C, was added dropwise a solution of methyl ester **44** (0.38 g, 1.24 mmol, dr = 10 : 1) in THF (7 ml). After 45 min at rt, the reaction was quenched with cold water (5 ml) and the layers were separated. The aqueous layer was extracted with Et_2O (3 × 20 ml) and the combined organic layers were washed with brine (10 ml), dried over $MgSO_4$, and concentrated *in vacuo*. The pale yellow residue was purified by column chromatography (SiO_2, hexanes–Et_2O 70 : 30) to give alcohol **45** (0.35 g, 1.24 mmol, 100%, dr = 10 : 1) as a colourless oil. The mixture of epimers was separated by further chromatography under the same conditions to **45** as a single diastereoisomer: $[\alpha]_D^{20}$ +55.4 (*c* 0.9, $CHCl_3$); ν_{max} film/cm^{-1} 3361 s, 2959 s, 2882 s, 1487 s, 1415 s, 1324 s, 1243 s, 1080 s, 1037 s, 922 m, 764 s; δ_H (400 MHz, $CDCl_3$): 6.83 (1H, s, C10H), 3.89 (3H, s, OMe), 3.81 (3H, s, OMe), 3.69 (1H, dd, *J* 7.4, 10.5, C2H), 3.62 (1H, dd, *J* 6.7, 10.5, C2H), 3.15–3.12 (1H, m, C6H), 3.03–2.98 (1H, m, C13H), 2.46–2.38 (1H, m, C3H), 2.22 (3H, s, C20H_3), 1.79 (1H, br s, OH), 1.75–1.52 (4H, m, C4H_2, C5H_2), 1.21 (3H, d, *J* 7.0, C19H_3), 0.72 (3H, d, *J* 6.8, C18H_3); δ_C (100 MHz, $CDCl_3$): 150.47, 148.76 (0, C7, C8), 135.56, 134.58 (0, C11, C12), 129.20 (0, C9), 124.22 (1, C10), 66.79 (1, C2), 60.38, 59.87 (3, 2 × OMe), 39.23, 38.17 (1, C6, C13), 28.97 (2, C5), 27.16 (1, C3), 21.82 (3, C19), 17.38 (2, C4), 16.04 (3, C20), 11.46 (3, C18); *m*/*z* (EI) 278 ($M^{+\bullet}$, 15%), 219 (100), 204 (5), 188 (10), 173 (5); Found: C, 73.40; H, 9.52%. $C_{17}H_{26}O_3$ (*M* = 278) requires C, 73.34; H, 9.41.

The minor epimer gave $[\alpha]_D^{20}$ +58.2 (*c* 1.1, $CHCl_3$); δ_H (400 MHz, $CDCl_3$): 6.88 (1H, s, C10H), 3.88 (3H, s, OMe), 3.81 (3H, s, OMe), 3.56 (1H, dd, *J* 4.7, 10.5, C2H), 3.42 (1H, dd, *J* 8.2, 10.5, C2H), 3.15–3.12 (1H, m, H6), 2.80–2.77 (1H, m, C13H), 2.44–2.38 (1H, m, C3H), 2.22 (3H, s, C20H_3), 1.74–1.52 (5H, m, C4H_2, C5H_2, OH), 1.20 (3H, d, *J* 7.0, C19H_3), 1.12 (3H, d, *J* 6.9, C18H_3); δ_C (100 MHz, $CDCl_3$): 150.68, 149.05 (0, C7, C8), 135.24, 134.52 (0, C11, C12), 129.34 (0, C9), 124.62 (1, C10), 65.18 (1, C2), 60.38, 59.89 (3, 2 × OMe), 41.08, 39.37 (1, C6, C13), 29.32 (2, C5), 27.34 (1, C3), 21.72 (3, C19), 18.95 (2, C4), 16.13 (3, C20), 16.07 (3, C18).

(5*S*,8*R*)-1,2-Dimethoxy-3,8-dimethyl-5-[(*R*)-1-methyl-2-(*p*-tolylsulfonyloxy)ethyl]-5,6,7,8-tetrahydronaphthalene (46)

To a solution of alcohol **45** (0.29 g, 1.04 mmol) in CH_2Cl_2 (7 ml) at 0 °C, was added successively DMAP (30 mg, 0.25 mmol), triethylamine (0.3 ml, 2.1 mmol) and toluene-*p*-sulfonyl chloride (0.30 g, 1.56 mmol). The reaction mixture was allowed to warm to rt and stirred for a further 5 h. The resulting mixture was diluted with Et_2O (30 ml), washed with HCl (2 M, 30 ml), sat. $NaHCO_3$ solution (30 ml), dried over $MgSO_4$ and concentrated *in vacuo*. The pale yellow residue was purified by column chromatography (SiO_2, hexanes–Et_2O 80 : 20) to afford tosylate **46** (0.43 g, 0.99 mmol, 96%) as white crystals: mp 102–104 °C (Et_2O–pentane); $[\alpha]_D^{18}$ +23.6 (*c* 1.1, $CHCl_3$); ν_{max} film/cm^{-1} 2949 s, 1612 s, 1492 m, 1372 s, 1195 s, 1104 m, 1084 m, 974 s, 807 s, 778 s, 677 m, 558 m; δ_H (400 MHz, $CDCl_3$): 7.84 (2H, d, *J* 8.3, H2′, H6′), 7.37 (2H, d, *J* 8.4, H3′, H5′), 6.64 (1H, s, C10H), 4.09–4.01 (2H, m, C2H_2), 3.87 (3H, s, OMe), 3.79 (3H, s, OMe), 3.14–3.07 (1H, m, C6H), 2.95–2.89 (1H, m, C13H), 2.60–2.50 (1H, m, C3H), 2.47 (3H, s, C7′H3), 2.19 (3H, s, C20H_3), 1.67–1.50 (2H, m, C4H_2 or C5H_2), 1.38–1.30 (2H, m, C4H_2 or C5H_2), 1.15 (3H, d, *J* 7.0, C19H_3), 0.68 (3H, d, *J* 6.9, C18H_3); δ_C (100 MHz, $CDCl_3$): 150.51, 148.95 (0, C7, C8), 144.89 (0, C1′), 135.47, 133.34, 133.26 (0, C11, C12, C4′), 130.13 (1, C2′, C6′), 129.35 (0, C9), 128.05 (1, C3′, C5′), 124.00 (1, C10), 73.69 (2, C2), 60.31, 59.80 (3, 2 × OMe), 37.61, 36.10 (1, C13, C6), 28.67 (2, C5), 27.00 (1, C3), 21.78 (3, C19), 21.70 (3, C7′), 17.07 (2, C4), 15.97 (3, C20), 11.07 (3, C18); *m*/*z* (EI) 432 ($M^{+\bullet}$, 20%), 260 (5), 219 (100), 188 (5), 173 (5), 91 (5); Found: C, 66.51; H, 7.45%. $C_{24}H_{32}O_5S$ (*M* = 432) requires C, 66.64; H, 7.46.

(5*R*,8*R*)-1,2-Dimethoxy-3,8-dimethyl-5-[(1*S*,3*RS*)-1,5-dimethyl-3-*p*-tolylsulfonylhex-4-enyl]-5,6,7,8,-tetrahydronaphthalene (49a,b)

To a solution of (3-methylbut-2-enyl) *p*-tolyl sulfone **48** (0.89 g, 3.95 mmol) in THF (7 ml) at −78 °C was added dropwise BuLi (2.32 M in hexane, 1.7 ml, 3.86 mmol) over 5 min. The resulting yellow–brown solution was allowed to warm to −50 °C over 1 h, and then cooled to −78 °C. A solution of tosylate **46** (0.43 g, 0.99 mmol) in THF (5 ml) was added dropwise to the mixture, and then allowed to warm to rt. After 4.5 h, the reaction mixture was diluted with Et_2O (25 ml) and washed with water (5 ml). The aqueous layer was extracted with Et_2O (2 × 20 ml) and the combined organic layers were washed with brine (10 ml), dried over $MgSO_4$ and concentrated *in vacuo*. The pale yellow residue was purified by column chromatography (SiO_2, hexanes–Et_2O 80 : 20) to give a mixture of allylic sulfones **49a**,**b** (0.44 g, 0.91 mmol, 92%, dr = 1 : 1) as a colourless solid: mp 51–54 °C; ν_{max} film/cm^{-1} 2939 s, 2882 s, 2259 m, 1612 m, 1497 s, 1454 s, 1420 s, 1382 s, 1320 s, 1243 s, 1147 s, 1085 s, 931 s, 821 m, 740 s, 668 s, 586 s; δ_H (400 MHz, $CDCl_3$): 7.72 (0.5 × 2H, d, *J* 8.1, H2′, H6′), 7.71 (0.5 × 2H, d, *J* 8.1, H2′, H6′), 7.31 (2H, d, *J* 7.9, H3′, H5′), 6.67 (0.5 × 1H, s, C10H), 6.56 (0.5 × 1H, s, C10H), 5.04 (0.5 × 1H, dd, *J* 1.1, 10.3, C14H), 4.97 (0.5 × 1H, dd, *J* 1.1, 10.3, C14H), 3.87 (3H, s, OMe), 3.85–3.80 (1H, m, C1H), 3.78 (3H, s, OMe), 3.12 (1H, br d, *J* 5.0, C6H), 2.75–2.72 (0.5 × 1H, m, C3H), 2.64–2.61 (0.5 × 1H, m, C3H), 2.44 (3H, s, C7′H3), 2.27–2.22 (2H, m, C2H_2), 2.19 (0.45 × 3H, s, C20H_3), 2.18 (0.55 × 3H, s, C20H_3), 1.75 (0.5 × 3H, s, C16H_3), 1.73 (0.5 × 3H, s, C16H_3), 1.70–1.62 (4H, m, C4H_2, C5H_2), 1.22 (3H, br s, C17H_3), 1.17 (0.5 × 3H, d, *J* 6.9, C19H_3), 1.16 (0.5 × 3H, d, *J* 6.9, C19H_3), 0.67 (0.5 × 3H, d, *J* 5.7, C18H_3), 0.61 (0.5 × 3H, d, *J* 5.4, C18H_3); δ_C (100 MHz, $CDCl_3$): 150.37, 150.29, 148.77, 148.69 (0, C7, C8), 144.34, 144.30 (0, C1′), 142.25, 142.0. (0, C15), 135.62, 135.47, 135.20, 135.14, 134.47, 134.,45 (0, C11, C12, C4′), 129.42, 129.39, 129.31, 129.30 (1, C2′, C3′, C5′, C6′), 129.20, 129.08 (0, C9), 124.15, 123.85 (1, C10), 117.84, 117.67 (1, C14), 63.81, 63.31 (1, C1), 60.27, 59.75 (3, 2 × OMe), 42.47, 38.60 (1, C3), 33.76, 33.47 (1, C13), 32.75, 31.96 (2, C2), 29.03, 28.98 (2, C5), 27.08 (1, C6), 25.96 (3, C16), 21.71 (3, C7′), 21.58, 21.31 (3, C19), 18.26, 18.17 (3, C17), 17.56, 16.30 (2, C4), 16.06, 16.04 (3, C20), 15.44, 13.24 (3, C18); *m*/*z* (EI) 484 ($M^{+\bullet}$, 15%), 329 (30), 278 (5), 246 (25), 219 (100), 191 (25), 123 (15), 84 (20), 41 (10); Found: C, 71.83; H, 8.36%. $C_{29}H_{40}O_4S$ (*M* = 484) requires C, 71.86; H, 8.32.

(1*R*,3*S*,6*R*,13*R*)-7,8-Dimethoxy-3,6,9-trimethyl-1-(2-methyl-prop-1-enyl)-2,3,3a,4,5,6-hexahydro-1*H*-phenalene [(+)-50b]

To a solution of sulfones **49a**,**b** (0.33 g, 0.68 mmol) in CH_2Cl_2 (15 ml) at −78 °C, was added dropwise $EtAlCl_2$ (1.0 M in hexane, 1.7 ml, 1.70 mmol). The resulting clear yellow reaction mixture was allowed to warm to −40 °C over 30 min, and then maintained at −40 °C for a further 4 h before being quenched with sat. $NaHCO_3$ solution (5 ml). The resulting white slurry was extracted with Et_2O (3 × 20 ml) and the combined organic layers were washed with brine (10 ml), dried over $MgSO_4$, and concentrated *in vacuo*. The pale yellow residue was purified by column chromatography (SiO_2, hexanes–Et_2O 98 : 2) to give pseudopterosin G–J aglycone dimethyl ether **50b** (0.20 g, 88%, dr >95 : 5) as a colourless oil. The single desired diastereoisomer was obtained as colourless crystals after crystallisation from MeOH: mp 107–109 °C; $[\alpha]_D^{18}$ +106.2 (*c* 1.0, $CHCl_3$); ν_{max} film/cm^{-1} 2939 s, 2863 s, 1473 s, 1420 s, 1387 m, 1324 s, 1257 m, 1085 s, 922 m, 744 m; δ_H (400 MHz, $CDCl_3$): 5.14 (1H, dd, *J* 1.3, 9.3, C14H), 3.89 (3H, s, OMe), 3.78 (3H, s, OMe), 3.64 (1H, br dt, *J* 3.4, 9.3, C1H), 3.24 (1H, quin, *J* 6.5, C6H), 2.08–2.03 (1H, m, C13H), 2.05 (3H, br s, C20H_3), 1.97 (1 H, dq, *J* 3.3, 12.6, C4H_{eq}), 1.87 (1H, ddt, *J* 2.8, 5.8, 13.2, C5H_{ax}), 1.79–1.77 (1H, m, C5H_{eq}), 1.75 (3H, d, *J* 1.0, C17H_3), 1.73–1.65 (3H, m, C2H_2

and C3H), 1.68 (3H, d, *J* 0.8, C16H$_3$), 1.46 (1H, dq, *J* 2.6, 12.6, C4H$_{ax}$), 1.21 (3H, d, *J* 6.9, C19H$_3$), 1.02 (3H, d, *J* 5.6, C18H$_3$); δ_C (100 MHz, CDCl$_3$): 149.27, 149.13 (0, C7, C8), 134.27, 133.30, 131.54, 129.38, 128.47 (0, C9, C10, C11, C12, C15), 130.97 (1, C14), 60.54, 60.08 (3, 2 × OMe), 46.32 (1, C13), 41.03 (2, C2), 36.15 (1, C1), 31.05 (2, C5), 29.71 (1, C3), 28.30 (1, C6), 25.79 (3, C16), 23.97 (3, C19), 22.59 (2, C4), 20.88 (3, C18), 17.84 (3, C17), 11.05 (3, C20); *m*/*z* (EI) 328 ($M^{+\bullet}$, 100%), 313 (75), 271 (15), 257 (20), 246 (15), 229 (10), 215 (5), 199 (5); Found: C, 80.41; H, 9.86%. $C_{22}H_{32}O_2$ (*M* = 328) requires C, 80.44; H, 9.82.

Ethyl (*E*,4*S*)-4-[(2,3-dimethoxy-4-methyl)phenyl]pent-2-enoate [(*S*)-22]

To a solution of 2,3-dimethoxy-4-methyl-1-iodobenzene **30** (3.93 g, 14.1 mmol) in THF (50 ml) at −90 °C was added dropwise BuLi (1.40 M in hexane, 10.6 ml, 14.8 mmol). The mixture was stirred at −78 °C for 15 min whereupon a solution of CuBr·SMe$_2$ (2.9 g, 14.1 mmol) in diisopropyl sulfide (3 ml) and THF (3 ml) was added dropwise whilst maintaining the temperature below −75 °C. The mixture was stirred at −78 °C for 45 min, cooled to −90 °C and solid complex **53** (1.35 g, 3.53 mmol) added portionwise keeping the temperature below −70 °C. After the addition, the reaction temperature was allowed to warm slowly to 0 °C over 5 h to give an orange mixture. An aqueous solution of ceric ammonium nitrate (1 M, 10 ml) was added and the mixture was allowed to warm to rt over 8 h. The reaction mixture was diluted with Et$_2$O (50 ml), the phases were separated and the aqueous layer was extracted with Et$_2$O (2 × 30 ml). The combined extracts were washed with sat. aq. NH$_4$F solution (30 ml), 10% NaHSO$_4$ solution (50 ml), brine (40 ml), dried over MgSO$_4$ and concentrated *in vacuo*. The rusty coloured residue was purified by column chromatography (SiO$_2$, hexanes–Et$_2$O 90 : 10) to give ethyl ester (*S*)-**22** (0.67 g, 2.40 mmol, 68%) as a colourless oil: $[\alpha]_D^{23}$ −69.2 (*c* 1.6, CHCl$_3$); ν_{max} film/cm^{-1} 2988 s, 1721 s, 1653 m, 1469 s, 1411 s, 1280 s, 1180 s, 1028 s, 918 s, 818 m; δ_H (400 MHz, CDCl$_3$): 7.12 (1H, dd, *J* 15.7, 6.2, C5H), 6.88 (1H, d, *J* 7.9, C11H), 6.78 (1H, d, *J* 7.9, C10H), 5.79 (1H, dd, *J* 15.7, 1.7, C4H), 4.18 (2H, q, *J* 7.1, OC*H*$_2$CH$_3$), 4.01–4.04 (1H, m, C6H), 3.85 (3H, s, OMe), 3.83 (3H, s, OMe), 2.25 (3H, s, C20H$_3$), 1.38 (3H, d, *J* 7.0, C19H$_3$), 1.28 (3H, t, *J* 7.1, OCH$_2$C*H*$_3$); δ_C (100 MHz, CDCl$_3$): 166.96 (0, C13), 153.11 (1, C5), 151.51, 150.67 (0, C7, C8), 135.11, 130.91 (0, C9, C12), 125.88, 122.36 (1, C10, C11), 119.93 (1, C4), 60.76 (3, OMe), 60.28 (2, O*C*H$_2$CH$_3$), 59.93 (3, OMe), 35.00 (1, C6), 19.86 (3, C19), 15.76 (3, C20), 14.34 (3, OCH$_2$*C*H$_3$); *m*/*z* (EI) 278 ($M^{+\bullet}$, 100%), 265 (8), 249 (12), 233 (28), 217 (35), 205 (65), 189 (78), 173 (45); Found: C, 69.03; H, 7.92%. $C_{16}H_{22}O_4$, (*M* = 278) requires C, 69.04; H, 7.97.

(5*R*,8*S*)-1,2-Dimethoxy-3,8-dimethyl-5-(2-trimethylsilylethynyl)-5,6,7,8-tetrahydronaphthalene [(−)-41a]

Silylalkyne (−)-**41a** derived from (*S*)-**22** as depicted in Schemes 5 and 6 gave mp 57.5–58.5 °C; $[\alpha]_D^{25}$ −50.2 (*c* 1.0, CHCl$_3$). The absolute stereochemistry of (−)-**41a** (Fig. 1) was confirmed by X-ray crystallography with Mo X-rays on a CAD4 diffractometer.[53,54] Crystal data (−)-**41a**¶¶ $C_{19}H_{28}O_2Si$, *M* = 316.50, monoclinic, *a* = 10.4402(9), *b* = 8.4616(8), *c* = 11.6528(15) Å, β = 103.300(9)°, *U* = 1001.8(2) Å^3, *T* = 293 K, space group $P2_1$, *Z* = 2, μ(Mo-Kα) 0.12 mm^{-1}. The full sphere of 9341 reflections with θ (Mo-Kα) < 28° were measured, and 4816 unique F^2 values (R_{int} = 0.0298) were used in refinement. *R*1 = 0.0910 and w*R*2 = 0.13 for all 4816 reflections. For 2947 reflections with $I > 2\sigma(I)$] *R*1 = 0.0431. The unique data set which contained 2252 Friedel pairs, gave an unambiguous determination of the absolute configuration. The structure shown in Fig. 1 gave a Flack parameter *x* = −0.07(15).

¶¶ CCDC reference number 168190.

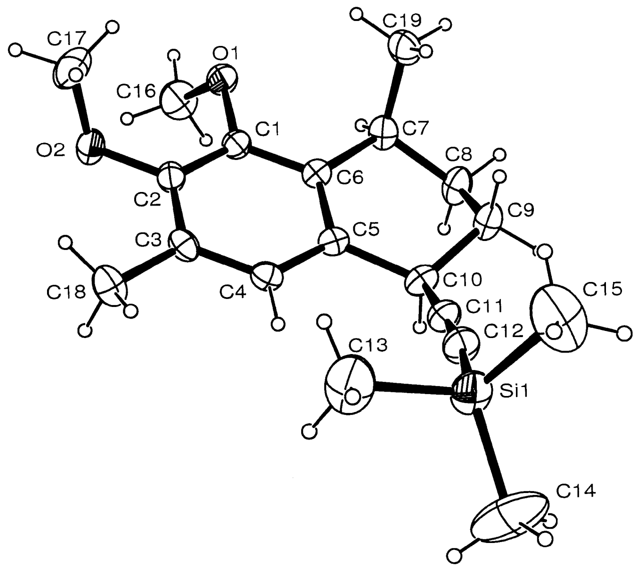

Fig. 1 Molecular drawing of (−)-**41a** showing the 50% probability ellipsoids for non-hydrogen atoms.

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