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Asymmetric Synthesis of (+)-Galbelgin, (−)-Kadangustin J, (−)-Cyclogalgravin and (−)-Pycnanthulignenes A and B, Three Structurally Distinct Lignan Classes, Using a Common Chiral Precursor

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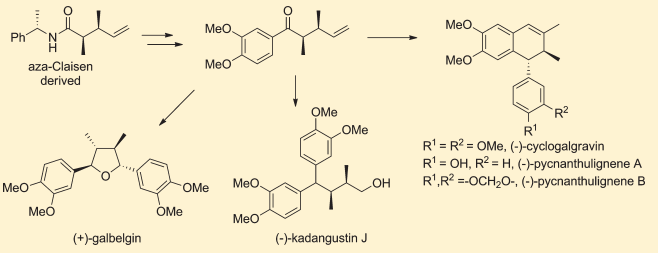
Supporting Information

ABSTRACT: The enantioselective synthesis of three structurally distinct classes of lignan from a single, aza-Claisen-derived, chiral morpholine amide is reported. The class of lignan formed is dependent on the substitution pattern in the aryl rings and choice of protecting group on a key benzylic hydroxyl group. The methodology has been used to asymmetrically synthesize and determine the absolute stereochemistry of lignans (+)-cyclogalgravin **3**, (−)-pycnanthulignene A **4**, (−)-pycnanthulignene B **5**, and (−)-kadangustin J **8**.



INTRODUCTION

Lignans are secondary plant metabolites formed by the oxidative dimerization of two phenylpropanoid units and have been found in roots, stems, leaves, seeds, and fruits in more than 70 plant families.[1] Though they may consist of only two phenylpropane (C_6-C_3) units, they have extremely diverse structures, with diversity mainly originating from the various linkage and oxidation patterns.[1] The natural biological function of most plant lignans is unknown; however, they have been discovered to have a vast array of interesting biological properties. While antimicrobial, antifungal, and insecticidal properties may be associated with plant defense it is their antitumor, anti-inflammatory, cardiovascular, and antioxidant properties among others that have spurred significant biological and synthetic interest.[1]

Lignans are traditionally classified as either classical lignans, where the phenylpropane dimers are linked in a $\beta-\beta'$ (8−8′) fashion, or neolignans, whose dimers have linkages other than $\beta-\beta'$. Examples of classical lignans include the tetrahydrofuran lignans (Figure 1) such as (+)-galbelgin **1**[2] and (+)-grandisin **2**,[3] along with the dihydroarylnapthalenes such as (−)-cyclogalgravin **3**[4] and the recently discovered pycnanthulignenes A **4** and B **5**.[5] Examples of neolignans include the 3′,7-epoxy-8,4′-oxyneolignan[6] (more commonly known as 1,4-benzodioxane lignans) eusiderins E **6** and G **7**[7] and the rearranged 1,1-diarylbutane lignan, kadangustin J **8**.[8]

Previously we have reported the racemic synthesis of tetrahydrofuran lignans,[9] and during that study we discovered that alteration of protecting groups and changes in aryl substitution led to unexpected products being formed. We herein report our findings in this area and show how a single precursor can be converted into three structurally diverse classes of lignan and in the process achieve the first asymmetric synthesis of cyclogalgravin (**3**), pycnanthulignene A (**4**), pycnanthulignene B (**5**), and kadangustin J (**8**).

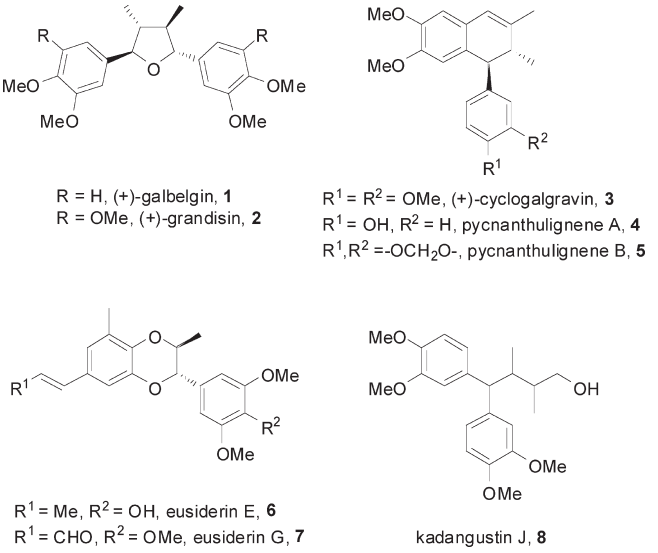


Figure 1. Diverse structures of natural lignans and neolignans.

RESULTS AND DISCUSSION

We have previously shown[9] that racemic, acyl-Claisen-derived, morpholine amide **9** could be converted into ketone **10**,

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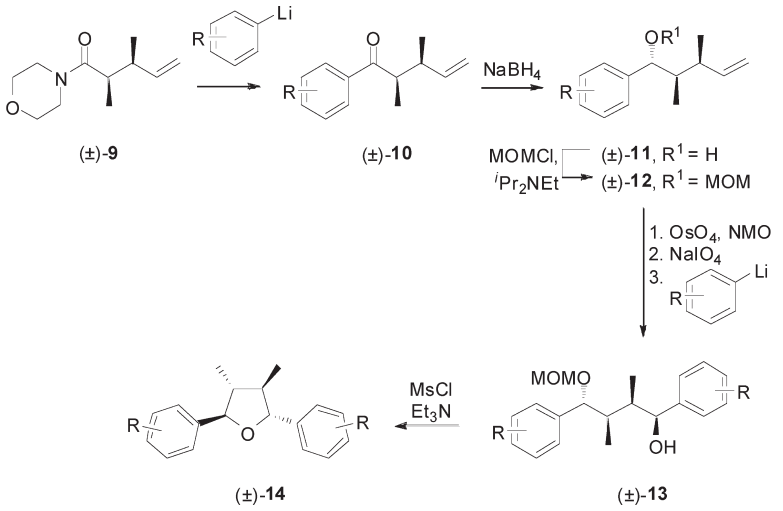
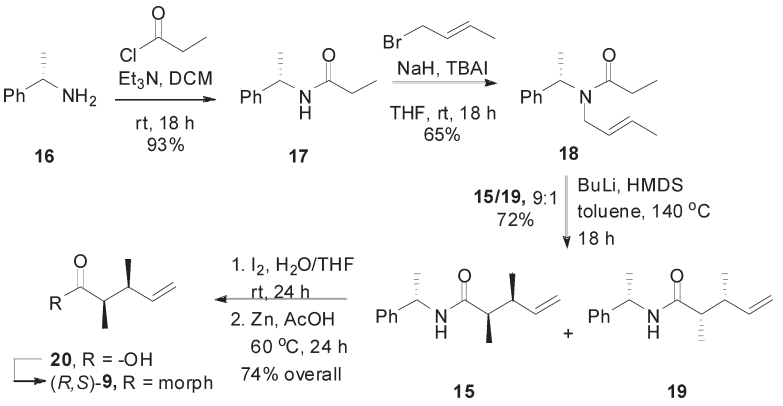
Scheme 1. Synthesis of Racemic Tetrahydrofurans



Scheme 2. Synthesis of Chiral Morpholine Amide 9



which after stereoselective reduction gave alcohol **11**, which was then protected as the MOM ether **12** (Scheme 1). Conversion of the terminal alkene to an aldehyde and addition of an aryllithium reagent gave alcohol **13**. In the key step, mesylation of alcohol **13** resulted in cyclization to give tetrahydrofuran lignans **14** in excellent yields.[9]

With this non-enantioselective methodology established we wished to apply this protocol to the asymmetric synthesis of a series of tetrahydrofuran lignans and thus required the synthesis of enantiomerically pure amide **9**. The synthesis of amide **9** begin with preparation of the reported chiral amide **15**.[10] Thus, (*S*)-α-methylbenzylamine **16** was acylated with propionyl chloride to give amide **17** in 93% yield (Scheme 2), which was then alkylated with (*E*)-crotylbromide, using NaH and TBAI in THF, to give amide **18** in 65% yield. Amide **18**, when treated with LiHMDS in toluene at 140 °C, underwent an aza-Claisen rearrangement[10,11] to give *syn*-dimethylamide **15** in 65% yield, along with 7% of the other, easily separable diastereoisomer **19**. Use of this aza-Claisen rearrangement was preferred over other chiral Claisen rearrangement[12] variants due to the very high level of stereoselectivity for the *syn*-dimethyl acid derivative **15**, with none of the *anti* diastereoisomers being observed on any occasion. While Tsunoda et al. have reported[13] the use of acetoxypivalimides for the hydrolysis of *N*-monosubstituted carboxamides of this type, we found iodolactonization followed by reductive ring opening using zinc in refluxing acetic acid[14] was more successful, giving acid **20** in 75% yield over two steps. Finally coupling of acid **20** with morpholine using DCC and DMAP gave (*R*,*S*)-dimethyl morpholine amide **9** in 73%.

Addition of lithiated 4-bromoveratrole **21** to (*R*,*S*)-**9** gave ketone **22**, which was reduced with sodium borohydride at −78 °C to give alcohol **23** as a single diastereoisomer in 74% yield, over two steps (Scheme 3). Alcohol **23** was then protected as the MOM ether before the terminal alkene was converted, via dihydroxylation followed by sodium periodinate cleavage, to give aldehyde **24** in 70% yield over three steps. Addition of lithiated 4-bromoveratrole **21** to aldehyde **24** at −78 °C gave alcohol **25** as a single diastereoisomer in 71% yield. Mesylation of alcohol **25** with 1.3 equiv of methanesulfonyl chloride along with 1.6 equiv of triethylamine activated the alcohol, deprotected the MOM ether, and gave (+)-galbelgin **1** in 59% yield in a single synthetic step. The spectral data and optical rotation of the synthetic material $[\alpha]_D$ = +81.8 (*c* 1.5, $CHCl_3$) matched reported literature values [$[\alpha]_D$ = +80.7 (*c* 0.55, $CHCl_3$)].[2a]

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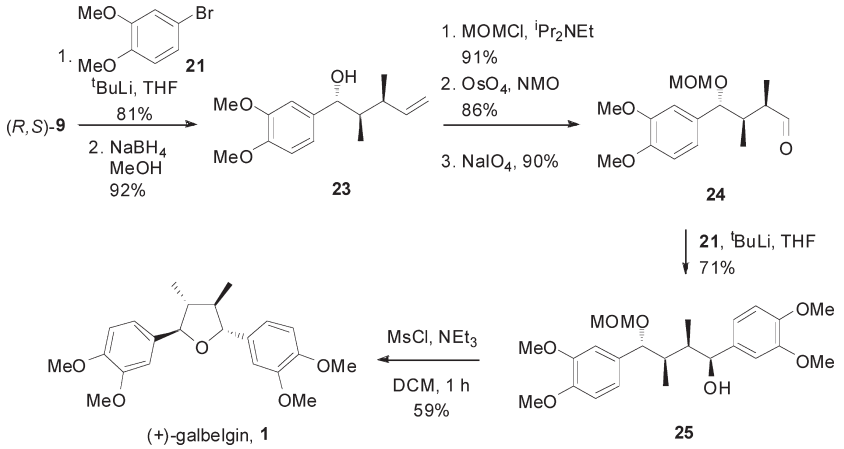
Scheme 3. Synthesis of (+)-Galbelgin



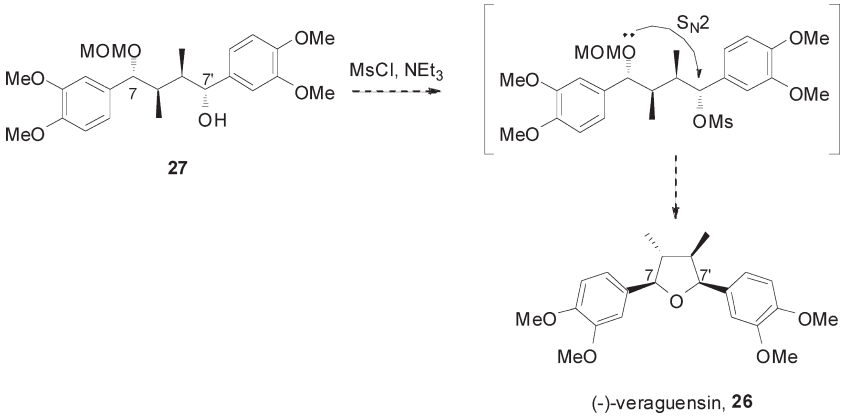


Figure 2. Proposed synthesis of (−)-veraguensin **26**.

We next wished to explore the synthesis of the related tetrahydrofuran lignan (−)-veraguensin **26**, which differs from galbelgin **1** only in that the stereochemistry of the substituents around the tetrahydrofuran in **26** are *trans,trans,cis* rather than the *trans,trans,trans* found in galbelgin **1**. We envisaged this could be accomplished by cyclizing alcohol **27**, which has inverted stereochemistry at the C-7′ (carbons numbered using lignan nomenclature). Activation of alcohol **27**, as the mesylate, followed by S_N2 attack of the C-7 hydroxyl group would result in the formation of (−)-veraguensin **26** (Figure 2).

We have observed[9] that using our optimized cyclization conditions on similar alcohols, such as **28**, where the C-7′ hydroxyl group is *anti* to the adjacent methyl group results in the formation of both the desired *trans,trans,cis* product **29** and the *trans,trans,trans* product **30**, in a 1.6:1 ratio. The unwanted production of the *trans,trans,trans* product **30** is believed to occur by the formation of a planar quinone methide intermediate **31**, where electron donation from the *para* oxygenated substituent results in elimination of the C-7′ mesylate with subsequent loss of stereochemistry (Scheme 4).[15]

Attack of the C-7 hydroxyl group on C-7′ is then non-stereospecific, resulting in mixtures of isomers being formed. The fact that epimeric products are not formed from the cyclization of alcohols such as **25** shows that competing mechanisms are in place. If a quinoid intermediate, such as **31**, is formed exclusively in all cases, then one might expect some (−)-veraguensin **26** to have been produced from the cyclization of alcohol **25**.

In order to further explore this cyclization step we wished to determine whether the C-7′ mesylates formed retained the stereochemistry of the original alcohol or epimerization was occurring during their formation. This required altering the protecting group of the C-7 hydroxyl group, as the C-7 MOM ether participated in the cyclization under the mesylate forming conditions. We began our investigation using racemic alcohol **32**, prepared in 83% yield over 2 steps from racemic amide **9** by addition of lithiated 4-bromoanisole and reduction of the newly formed ketone (Scheme 5). We decided upon the TBDMS ether, as benzylic TBDMS ethers have been shown to be stable to mesylation conditions.[16] Thus, alcohol **32** was converted to ether **33** in 87% yield, which followed by dihydroxylation and oxidative cleavage gave aldehyde **34** in 69% yield over two steps. Addition of lithiated 4-bromoanisole at −78 °C gave alcohol **35** again as a single diastereoisomer in 92% yield. Mesylation of alcohol **35**, however, unexpectedly gave aldehyde **36** in 85% yield.

The net result of the reaction is a 1,4-aryl shift along with loss of *tert*-butyldimethylsilanol. One plausible mechanism for the synthesis of **36** involves initial formation of the quinoid intermediate **37**; however, in this case the generated HCl does not cleave the O−Si bond leading to the formation of an O-centered

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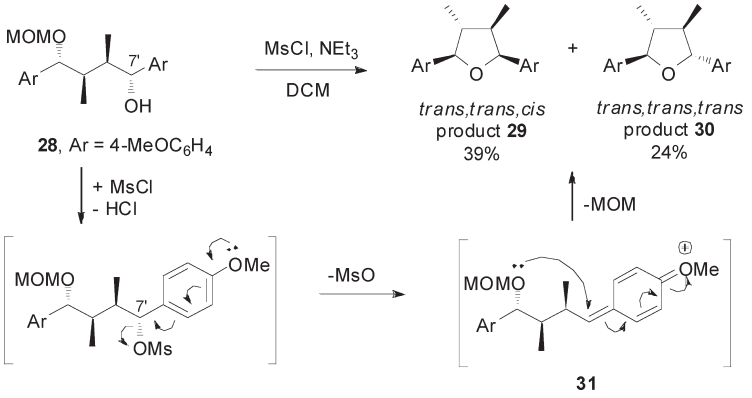
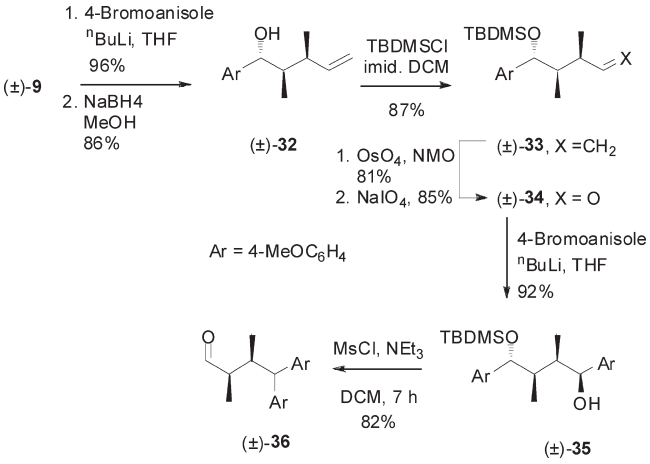
Scheme 4. Proposed Mechanism for the Isomerization of Tetrahydrofurans



Scheme 5. Synthesis of Aldehyde 36



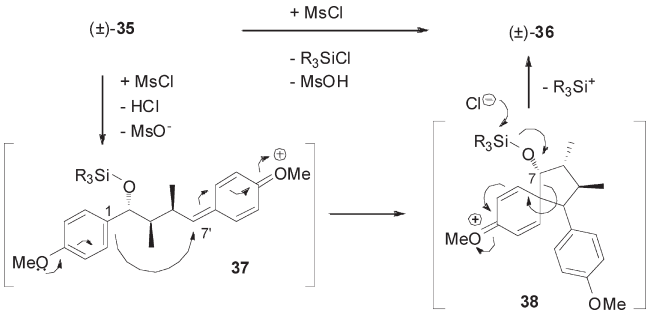


Figure 3. Proposed mechanism for the formation of aldehyde **36**.

nucleophile. Instead *ipso* attack of C-1, via donation from the *p*-methoxy group, on C-7′ leads to the formation of cyclopentyl intermediate **38**. Cleavage of the O−Si bond then results in the formation of aldehyde **36** with re-aromatization being the driving force (Figure 3).

It was after this result that we noticed the similarity of the formed aldehyde **36** to the recently isolated lignan, kadangustin J **8**,[8] which differed only in the extra methoxy groups on the two aryl rings. While kadangustin J **8** was reported to be optically active $[\alpha]_D$ = +4.9 (*c* 0.171, MeOH)] the stereochemistry of the

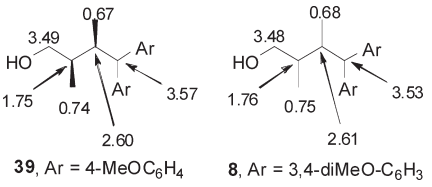


Figure 4. Comparison of ^{1}H NMR chemical shift (δ ppm) between **8** and **39**.

methyl substituents was unreported, and we considered whether this unexpected rearrangement could be applied to the synthesis and stereochemical determination of kadangustin J **8**.

Initially we wished to see if aldehyde **36** could assist with determining the relative stereochemistry of kadangustin J **8**. Thus aldehyde **36** was reduced with $NaBH_4$ to give alcohol **39** in 64% yield. Comparison of the reported ^{1}H NMR spectra of kadangustin J **8** with alcohol **39** showed similarities in both the chemical shift and coupling constants of protons at C-7, -7′, -8, -8′, -9 and -9′, strongly suggesting kadangustin J **8** had the same *syn*-dimethyl stereochemistry found in alcohol **39** (figure 4).

With this knowledge we turned our attention to the asymmetric synthesis of kadangustin J **8**, which began by protecting chiral alcohol **23** as the TBDMS ether **40**, which was then converted to aldehyde **41** before addition of lithiated 4-bromoveratrole **21** gave the desired alcohol **42** in an overall 41% yield, over 4 steps from **23** (Scheme 6). With the desired alcohol **42** in hand we then attempted the mesyl chloride induced rearrangement to form aldehyde **43**. However in this case rather than aldehyde **43** being formed, another class of lignan, dihydroarylnapthalene (−)-**3**, also known as (−)-cyclogalgravin,[16] was generated instead as a single stereoisomer in 95% yield.

The spectral data and optical rotation, $[\alpha]_D$ = −128.0 (*c* 0.2, $CHCl_3$), of the purified synthetic product matched the reported literature value, $[\alpha]_D$ = −105.9 (*c* 1.07, $CHCl_3$),[17] and was opposite that of of the previously isolated enantiomer, $[\alpha]_D$ = +135.5 (*c* 0.28, $CHCl_3$).[4b] All other syntheses of cyclogalgravin **3** have been semisynthetic, using isolated tetrahydrofuran lignans as starting materials[18] and therefore this work constitutes the first asymmetric total synthesis of either enantiomer of cyclogalgravin **3**.

Mechanistically the synthesis of (−)-**3** can be explained by the attack of C-6, which in this case is *para* to the C-3 methoxy group, at C-7′, rather than *ipso* attack of C-1 seen in formation of

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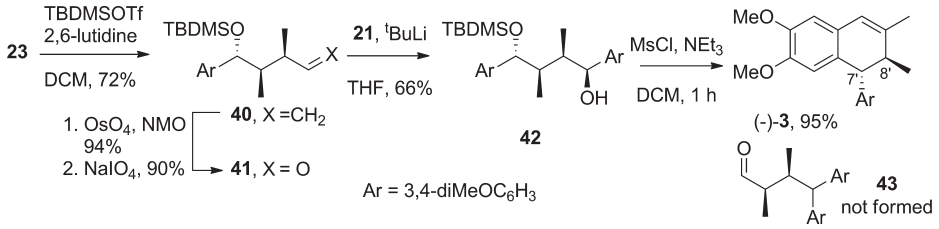
Scheme 6. Synthesis of (−)-Cyclogalgravin 3



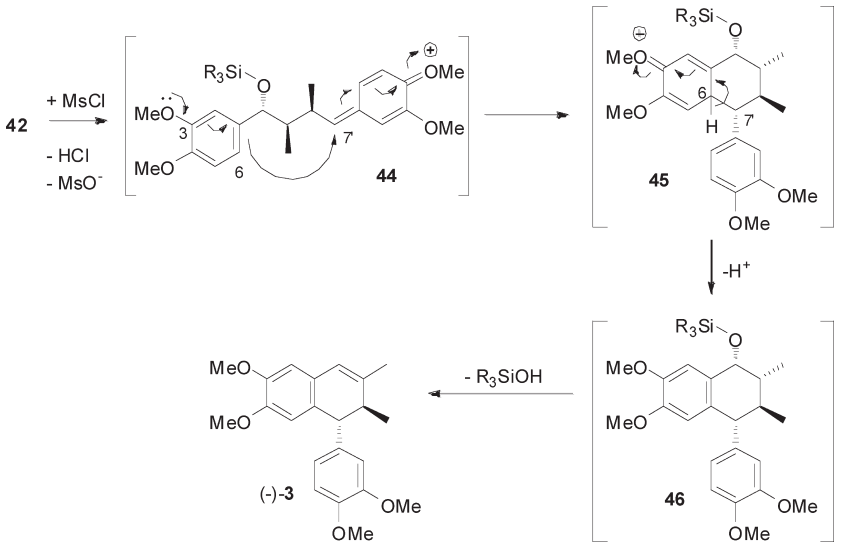


Figure 5. Proposed mechanism for the formation of (−)-cyclogalgravin **3**.

aldehyde **36**. The attack at C-7′ could have occurred by direct displacement of the newly formed mesylate or again by formation of a quinoid intermediate **44**. In either case the resultant intermediate **45** then rearomatizes to give tetrahydronaphthalene **46**, which then undergoes elimination of *tert*-butyldimethylsilanol to form the dihydroarylnaphthalene **3** (Figure 5). During the course of this work, a biosynthetic study was published[19] on aryltetralone lignans that proposes a similar mechanism for the formation of the arylnaphthalene ring system. This mechanism was further supported during our synthesis of pycnanthulignene B **5** when the equivalent intermediate to **46** was able to be isolated (see below).

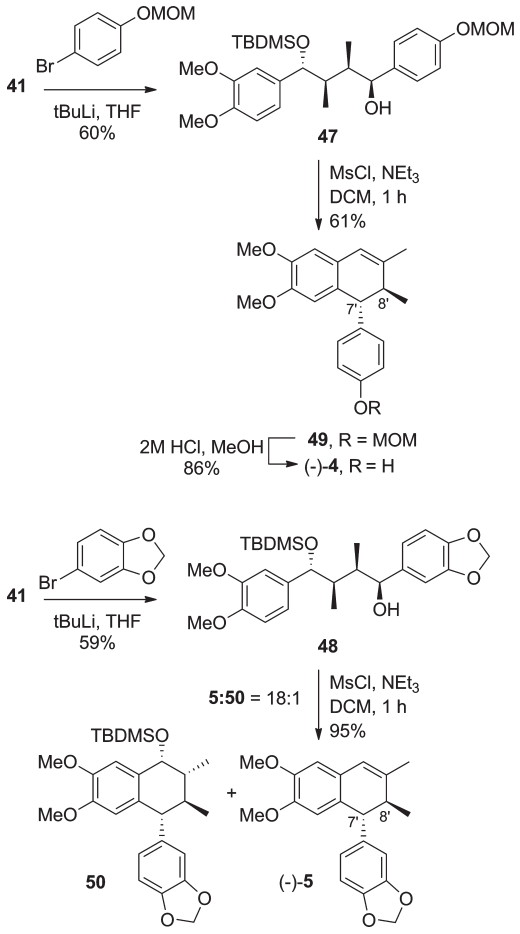
With the discovery that substrates such as **42** containing electron-donating groups at C-3 undergo this alternative pathway to form dihydroarylnaphthalenes, we looked for additional targets that would take advantage of this finding. The recently isolated[5] pycnanthulignene A **4** and pycnanthulignene B **5**, which show high levels of antimicrobial activity, are two such chiral dihydroarylnapthalenes in which the absolute stereochemistry of the natural products has not been determined.

Our synthesis of pycnanthulignenes A **4** and B **5** began from aldehyde **41**. Thus the lithiates of 1-bromo-4-(methoxymethoxy) benzene and 1-bromo-3,4-methylenedioxybenzene were added to aldehyde **41** and gave alcohols **47** and **48**, in 60% and 59% yields, respectively (Scheme 7). Treatment of alcohol **47** with mesyl chloride gave the predicted dihydroarylnaphthalene **49** in 61% yield. Deprotection of the MOM ether was achieved with aqueous HCl to give pycnanthulignene A **4** in 86% yield. The optical rotation of the synthetic product **4** was $[\alpha]_D = -41.0$ (*c* 0.16, EtOH), opposite in sign to natural product $[\alpha]_D = +33.8$ (*c* 0.31, EtOH),[5] thus determining the absolute stereochemistry of the natural pycnanthulignene A **4** to be 7′*S*,8′*R*. Similarly treatment of alcohol **48** with mesyl chloride gave the desired pycnanthulignene B **5** in 95% yield; however, in this case a small amount of the unstable intermediate **50** was isolated, which upon standing in $CDCl_3$ converted to **5** over the period of a few hours. The optical rotation of the synthetic product **5** was $[\alpha]_D = -100$ (*c* 0.58, EtOH), again opposite in sign to that of the isolated natural product, $[\alpha]_D = +118.5$ (*c* 0.338, EtOH),[5] thus determining the absolute stereochemistry of the natural pycnanthulignene B **5** to also be 7′*S*,8′*R*.

With a route to the dihydroarylnaphthalene lignans determined, we returned to the synthesis of kadangustin J **8**. Our alternative strategy involved addition of a second equivalent of lithiate **21** to ketone **22** to give tertiary alcohol **51**, which could then be dehydroxylated and the terminal alkene converted into the desired primary alcohol. Thus, addition of lithiated **21** to ketone **22** gave alcohol **51** in 68% yield (Scheme 8). With alcohol **51** in hand, methods for the dehydroxylation were then explored. Conversion of alcohol **51** into a sulfonate ester or chloride followed by reduction with $LiAlH_4$ were unsuccessful,[20] giving only degradation products. Eventually use of Et_3SiH and $BF_3 \cdot OEt_2$ in a dilute reaction mixture, using DCM at 0 °C, gave a 20:1 mixture of the desired alkane **52** along with dehydrated alkene **53** in overall 95% yield. The terminal alkene of **52** was then

converted to the desired primary alcohol by dihydroxylation and oxidative cleavage followed by $NaBH_4$ reduction and gave (8*S*,8′*R*)-kadangustin J **8** in 80% yield over 3 -steps. The ^1H and ^{13}C NMR data for the synthetic compound were identical to the reported data for the natural product. The optical rotation of the isolated synthetic product was $[\alpha]_D = -20.7$ (*c* 1.19, MeOH), larger in magnitude and opposite in sign to that of the natural product,[8] $[\alpha]_D = +4.9$ (*c* 0.171, MeOH) thus suggesting the absolute stereochemistry of the natural kadangustin J **8** to be (8*R*,8′*S*).

Scheme 7. Synthesis of (−)-Pycnanthulignene A (4) and B (5)



CONCLUSIONS

In conclusion the asymmetric synthesis of (+)-galbelgin **1** along with the first asymmetric syntheses of (−)-cyclogalgravin **3**, (−)-pycnanthulignenes A **4** and B **5**, and (−)-kadangustin J **8** has been achieved, with absolute stereochemistry of the natural pycnanthulignenes A **4** and B **5** and kadangustin J **8** being determined. A common chiral precursor, aza-Claisen-derived amide **9**, was the starting material for each of these structurally distinct lignans. Tetrahydrofuran products are formed from the precyclized intermediates when the C-7 hydroxyl group is protected as a MOM ether and mesyl chloride is added to activate the C-7′ hydroxyl group. However, when the C-7 hydroxyl group is protected with a TBDMS ether, dihydroarylnapthalenes are formed in the case when the adjacent aryl ring bears an electron-donating substituent at C-3, or if a donating substituent is only found at C-4, then a 1,4-aryl shift occurs to give rearranged products.

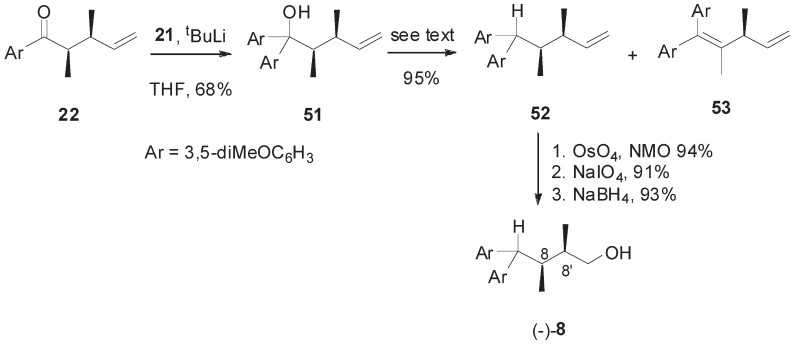
EXPERIMENTAL SECTION

All reactions sensitive to air or moisture were carried out under argon or nitrogen atmosphere in dry, freshly distilled solvents under anhydrous conditions unless otherwise noted. All NMR spectra were recorded on a 300 or 400 MHz spectrometer. Chemical shifts are reported relative to the solvent peak of chloroform (δ 7.24 for ^1H and δ 77.0 for ^{13}C). Signal patterns are indicated as s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad peak. NMR peak assignments were performed by COSY, HSQC, HMBC, and NOESY experiments. High-resolution mass spectroscopy (HRMS) was carried out in electrospray mode. All optical rotation measurements were determined at 20 °C on the sodium D line (λ = 589 nm, 0.1 dm cell).

General Procedure A: Lithiate Addition of Disubstituted Aromatic Bromides. To a solution of the aromatic bromide (1.1 mmol) in THF (10 mL) under an atmosphere of nitrogen at −78 °C was added *tert*-butyllithium (1.5 M in pentane, 2.2 mmol), and the resultant solution was stirred for 10 min. A solution of the amide or aldehyde (1 mmol) in THF (10 mL) was then added dropwise, and the mixture was stirred at −78 °C for 1 h before being allowed to warm to room temperature and stirring overnight. Saturated NH_4Cl solution (20 mL) was added, and the aqueous mixture was extracted with ethyl acetate (3 × 20 mL). The combined organic extracts were washed with brine (40 mL) and dried ($MgSO_4$), and the solvent was removed *in vacuo*. The crude product was purified by flash chromatography to afford the product.

General Procedure B: Ketone or Aldehyde Reduction to an Alcohol. To a solution of ketone or aldehyde (1 mmol) in methanol (5 mL) at −78 °C was added sodium borohydride (4 mmol), and the resulting suspension was stirred under an atmosphere of nitrogen at

Scheme 8. Synthesis of (−)-Kadangustin J



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room temperature for 6 h. Water (5 mL) was added, and the methanol was removed *in vacuo*. Further water (5 mL) was added to the residue, and the crude product was extracted with ethyl acetatae (3 × 15 mL). The combined organic extracts were dried ($MgSO_4$), the solvent was removed *in vacuo*, and the crude product was purified by flash chromatography to afford the alcohol.

General Procedure C: Dihydroxylation of Terminal Alkene. To a stirred suspension of *N*-methylmorpholine-*N*-oxide (3 mmol) in a 1:1 water/*tert*-butanol mixture (10 mL) was added the alkene (1 mmol). Osmium tetroxide (0.01 mmol, as a 2.5 g/100 mL solution in *tert*-butanol) was added dropwise and the resulting suspension was stirred at room temperature for 48 h. Saturated sodium sulphite solution (20 mL) was added and the mixture stirred for 1 h. The aqueous mixture was extracted with ethylacetate (3 × 30 mL) and the combined organic extracts were washed with 1 M KOH solution (50 mL) and dried ($MgSO_4$), and the solvent was removed *in vacuo*. The crude product was purified by flash chromatography to afford the corresponding diol.

General Procedure D: Periodate Cleavage of Diol to Aldehyde. To a stirred solution of diol (1 mmol) in a 3:1 methanol/water mixture (30 mL) was added sodium periodate (1.2 mmol), and the resultant suspension was stirred for 30 min. Brine (20 mL) was added, the mixture was extracted with ethyl acetate (3 × 50 mL), and the combined organic extracts were washed with water (2 × 50 mL) and dried ($MgSO_4$). The solvent was removed *in vacuo*, and the crude product was purified by flash chromatography to afford the corresponding aldehyde.

General Procedure E: Cyclization Using Methanesulfonyl Chloride. To a solution of alcohol (1 mmol) and triethylamine (1.6 mmol) in DCM (25 mL) under an atmosphere of nitrogen was added methanesulfonyl chloride (1.3 mmol), and the reaction mixture was stirred for 1−2 h. Saturated $NaHCO_3$ solution (10 mL) was added, the layers were separated, and the aqueous layer was further extracted with DCM (3 × 15 mL). The combined organic extracts were dried (Na_2SO_4), and the solvent was removed *in vacuo*. The crude product was purified by flash chromatography to afford the cyclized or alternative product.

(*S*)-*N*-(1-Phenylethyl)propanamide, 17. To a stirred solution of (*S*)-(1-phenylethyl) amine (5.0 g, 41 mmol) in DCM (50 mL) under an atmosphere of nitrogen was added triethylamine (11.4 mL, 82 mmol), and the resulting mixture was stirred for 10 min at 0 °C before propionyl chloride (3.9 mL, 45 mmol) was added dropwise. The resulting solution was stirred at room temperature for 18 h. Saturated NH_4Cl solution (20 mL) was added, the layers were separated, and the aqueous phase was further extracted with DCM (3 × 20 mL). The combined organic layers were washed with $NaHCO_3$ solution (30 mL) and dried ($MgSO_4$). The crude product was purified by flash chromatography (2:1 hexanes/ethyl acetate) to give the title product (6.7 g, 93%) as a white solid: mp 59−61 °C [lit.[21] 55−56 °C]; $[\alpha]_D$ = −170 (*c* 1.26, $CHCl_3$); δ_H (400 MHz; $CDCl_3$) 1.15 (3H, t, *J* = 8.0 Hz, 3-CH_3), 1.48 (3H, d, *J* = 8.0 Hz, 1′-CH_3), 2.21 (2H, q, *J* = 8.0 Hz, 2-CH_2), 5.13 (1H, q, *J* = 8.0 Hz, 1′-H), 5.79 (1H, br s, NH) and 7.32−7.33 (5H, m, Ar-H); δ_C (100 MHz; $CDCl_3$) 9.8 (CH_3, C-3), 21.8 (CH_3, C-1′), 29.8 (CH_2, C-2), 48.6 (CH, C-1′), 1262, 127.3, and 128.7 (CH, Ar-C), 143.4 (q, Ar-C) and 172.8 (C═O, C-1). The ^1H and ^{13}C NMR data were in agreement with the literature values.[21]

(*S*)-*N*-(But-2-enyl)-*N*-(1-phenylethyl)propanamide, 18. To a stirred suspension of NaH (3.2 g, 80 mmol (60% under kerosene) washed with pentane) in THF (60 mL) was added TBAI (0.73 g, 50 mmol), and mixture was placed under an atmosphere of nitrogen. Crotyl bromide (5.4 g, 40 mmol) was then added, and the mixture was cooled to 0 °C before amide **17** (7.0 g, 40 mmol) in THF (10 mL) was added dropwise. The resulting mixture was stirred at 0 °C for 1 h and then allowed to warm to room temperature overnight. The resultant solid was filtered off and washed with DCM (20 mL), the filtrate was concentrated *in vacuo*, and the residue was dissolved in ethyl acetate (30 mL). This was washed with brine (20 mL) and dried ($MgSO_4$). The crude product was purified by flash chromatography (2:1 hexanes/ethyl acetate) to give the title product (6.1 g, 65%) as a yellow oil: $[\alpha]_D$ = −9.4 (*c* 1.06, $CHCl_3$); ν_{max}(neat)/cm^{-1} 2974 and 2938 (CH), 1643 (C═C), 1449, 1416, 1376, 1205, 1178 and 1072, 964 and 699; δ_H (300 MHz; $CDCl_3$) 1.17 (3H, t, *J* = 9.0 Hz, CH_2CH_3), 1.49 (3H, d, *J* = 6.0 Hz, N-$CHCH_3$), 1.60 (3H, m, $CHCH_3$), 2.35 (2H, q, *J* = 9.0 Hz, CH_2CH_3), 3.38 −3.68 (2H, m, N-CH_2), 5.14−5.19 and 5.39−5.45 (2H, m, CH alkene), 6.08 (1H, q, *J* = 9.0 Hz, N-CH) and 7.25−7.32 (5H, m, Ar-H); δ_C (100 MHz; $CDCl_3$) 9.6 (CH_3, CH_2CH_3), 16.7 (CH_3, $NCHCH_3$), 17.6 (CH_3, $CHCH_3$), 45.3 (CH_2, N-CH_2), 50.9 (CH, N-CH), 126.7, 127.4, and 128.3 (CH, Ar-C), 141.3 (q, Ar-C) and 174.4 (C═O, N-C═O); *m*/*z* (EI) 231 (M^+, 10%), 176 (94), 120 (92), 105 (100), 70 (60); HRMS (EI) calcd for $C_{15}H_{21}NO$, 231.1623; found, 231.1626.

(2*R*,3*S*)-2,3-Dimethyl-*N*-((*S*)-1-phenylethyl)pent-4-enamide, 15. To a stirred solution of hexamethyldisilazane (0.23 mL, 1.0 mmol) in toluene (2 mL) cooled to 0 °C was added *n*-butyllithium (0.69 mL, 1.0 mmol, 1.6 M in *n*-hexanes), and the solution was stirred for 15 min before amide **18** (0.169 g, 0.7 mmol) in toluene (2 mL) was added dropwise. The pressure vessel was sealed and heated at 140 °C for 24 h. Reaction mixture was cooled to rt before water (10 mL) was added, the layers were separated, and the aqueous phase was further extracted with ethyl acetate (3 × 30 mL). The combined organic layers were dried ($MgSO_4$), and the solvent was removed *in vacuo*. The crude product was purified by flash chromatography (2:1 hexanes/ethyl acetate) to give the title product (0.11 g, 65%) as a yellow oil: $[\alpha]_D$ = −10.1 (*c* 0.68, $CHCl_3$); ν_{max}(neat)/cm^{-1} 3287 (NH), 2971 and 2931 (CH), 1638 (C═C), 1540, 1494, 1450, 1376, 1227, 997, 910 and 698; δ_H (400 MHz; $CDCl_3$) 0.99 (3H, d, *J* = 8.0 Hz, 3-CH_3), 1.06 (3H, d, *J* = 8.0 Hz, 2-CH_3), 1.42 (3H, d, *J* = 4.0, $NCHCH_3$), 2.08 (1H, m, 2-H), 2.40 (1H, q, *J* = 4.0 Hz, 3-H), 4.95−5.03 (2H, m, 5-CH_2), 5.09 (1H, m, NCH), 5.77 (1H, m, 4-H), 6.22 (1H, br s, NH) and 7.22−7.29 (5H, m, Ar-H); δ_C (100 MHz; $CDCl_3$) 14.5 (CH_3, C-2), 16.4 (CH_3, C-3), 21.6 (CH_3, $CHCH_3$), 40.6 (CH, C-3), 46.2 (CH, C-2), 48.1 (CH, NCH), 113.9 (CH_2, C-5), 126.0, 126.9, and 128.3 (CH, Ar-C), 141.7 (q, Ar-C), 143.3 (CH, C-4), and 174.3 (C═O, C-1); *m*/*z* (ESI) 254 (MNa^+, 50%) 232 (MH^+, 100), 128 (55), 105 (10); HRMS (ESI) calcd for $C_{15}H_{22}NO$, 232.1696; found, 232.1696. The minor diastereomer **19** was also obtained (0.012 g, 7%) as a yellow oil.

(2*R*,3*S*)-2,3-Dimethylpent-4-enoic, 20. To a stirred solution of (2*R*,3*S*)-2,3-dimethyl-*N*-((*S*)-1-phenylethyl)pent-4-enamide **15** (0.1 g, 0.45 mmol) in a 1:1 THF/water mixture (2 mL), excluded from light, was added iodine (0.25 g, 1.0 mmol), and the mixture was stirred at room temperature for 20 h. The solution was diluted with ether (10 mL), washed with saturated Na_2SO_5 solution (2 × 10 mL), and then dried ($MgSO_4$), and solvent was removed *in vacuo*, to afford the intermediate iodolactone (0.1 g, 91%) as a yellow oil that was used directly in the following reaction. To a stirred solution of iodolactone (0.1 g, 0.45 mmol) in acetic acid (2 mL) was added zinc dust (0.25 g, 3.9 mmol), and the mixture was stirred at 60 °C for 18 h. The mixture was quenched with 2 M HCl (5 mL) and diluted with ether (10 mL). The layers were separated, and the aqueous mixture further extracted with ether (3 × 10 mL) and dried ($MgSO_4$), and the solvent was removed *in vacuo*, to afford the title product (0.4 g, 69%) as a yellow oil. $[\alpha]_D$ = −0.9 (*c* 1.0, $CHCl_3$); ν_{max}(neat)/cm^{-1} 3354 (OH), 2968, 2923, and 2852 (CH), 1706 (C═O), 1456, 1229 and 914; δ_H (300 MHz; $CDCl_3$) 1.08 (3H, d, *J* = 9.0 Hz, CH_3), 1.14 (3H, *J* = 9.0 Hz, CH_3), 2.33−2.49 (2H, m, 2-H and 3-H), 5.03 (2H, m, 5-CH_2) and 5.67 (1H, m, 4-CH); δ_C (100 MHz; $CDCl_3$) 13.1 and 15.9 (2 × CH_3, C-2 and C-3), 40.0 and 44.5 (2 × CH, C-2 and C-3), 114.6 (CH_2, C-5), 141.1 (CH, C-4), 181.9 (C═O, C-1); The ^1H and ^{13}C NMR data were in agreement with the literature values.[12]

(2*R*,3*S*)-2,3-Dimethyl-1-morpholinopent-4-en-1-one, (*R*,*S*)-9. To a solution of acid **20** (2.7 g, 21 mmol) in DCM (20 mL) at 0 °C was added morpholine (2.0 mL, 23 mmol), followed by DMAP (0.64 g, 5.25 mmol) and DCC (4.7 g, 23 mmol). The resulting mixture was stirred under an atmosphere of nitrogen and allowed to warm to room temperature over 22 h. The mixture was filtered through a pad of Celite, washed with DCM (30 mL) followed by aqueous HCl (2M, 20 mL) and aqueous NaOH (1 M, 30 mL), then dried ($MgSO_4$), and the solvent was removed *in vacuo*. The crude product was purified by flash chromatography (2:1 hexanes/ethyl acetate) to afford the title product (3.1 g, 73%) as a yellow oil. $[\alpha]_D = -36.0$ (*c* 1.26, $CHCl_3$); δ_H (400 MHz; $CDCl_3$) 1.02 (3H, d, *J* = 4.0 Hz, 3-CH_3), 1.10 (3H, d, *J* = 4.0 Hz, 2-CH_3), 2.46 (1H, m, 3-H), 2.59 (1H, m, 2-H), 3.51−3.68 (8H, m, O(CH_2CH_2)$_2$N) and 4.99−5.04 (2H, m, 5-CH_2), 5.74 (1H, m, 4-H); δ_C (100 MHz; $CDCl_3$) 14.5 and 16.0 (2 × CH_3, 2-CH_3 and 3-CH_3), 40.1 (CH, C-2 and C-3), 42.0 and 46.3 (CH_2, O(CH_2CH_2)$_2$N), 66.8 and 67.1 (CH_2, O(CH_2CH_2)$_2$N), 114.0 (CH_2, C-5), 142.1 (CH, C-4) and 173.3 (q, C-1). The ^{1}H and ^{13}C NMR spectra were in agreement with literature values.[22]

(2*R*,3*S*)-1-(3,4-Dimethoxyphenyl)-2,3-dimethylpent-4-en-1-one, 22. The reaction was carried out according to general procedure A, using 4-bromoveratrole (0.52 g, 2.4 mmol) and *tert*-butyllithium (3.2 mL, 4.8 mmol, 1.5 M) with amide (*R*,*S*)-**9** (0.32 g, 1.6 mmol). A solvent mixture of 2:1 hexanes/ethyl acetate was used for flash chromatography to give the title product (0.32 g, 81%) as a pale yellow oil. $[\alpha]_D = -64$ (*c* 1.4, $CHCl_3$); ν_{max}(neat)/cm^{-1} 2968 and 2862 (CH), 1665 (C═O), 1581 and 1510 (C═C), 1454, 1345, 1257, 1197, 1148, and 1021 (C−O ether), 909, 852 and 764; δ_H (400 MHz; $CDCl_3$) 1.01 (3H, d, *J* = 8.0 Hz, 3-CH_3), 1.14 (3H, d, *J* = 4.0 Hz, 2-CH_3), 2.65 (1H, ddq, *J* = 8.0, 8.0, 8.1 Hz 3-H) 3.44 (1H, dq, *J* = 4.1, 8.0 Hz, 2-H), 3.94 (6H, s, 2 × OCH_3), 4.95 (2H, m, 5-CH_2), 5.81 (1H, m, 4-H), 6.90 (2H, d, *J* = 8.4 Hz, 5′-H), 7.53 (1H, d, *J* = 1.2 Hz, 2′-H) and 7.57 (1H, dd, *J* = 8.4, 1.6 Hz, 6′-H); δ_C (100 MHz; $CDCl_3$) 13.6 (CH_3, C-2), 15.7 (CH_3, C-3), 40.1 (CH, C-3), 44.7 (CH, C-2), 56.0 and 56.1 (CH_3, 2 × OCH_3), 109.9 (CH, C-2′), 110.6 (CH, C-5′), 113.9 (CH, C-6′), 122.6 (CH, C-4), 130.1 (q, C-1′), 142.2 (CH_2, C-5), 149.1 and 153.1 (q, C-4′ and C-5′) and 202.3 (C═O, C-1); *m*/*z* (EI) 248 (M$^+$, 20%), 192 (4), 165 (100), 79 (6), 77 (5); HRMS (EI) calcd for $C_{15}H_{20}O_3$, 248.1412; found, 248.1406.

(1*R*,2*R*,3*S*)-1-(3,4-Dimethoxyphenyl)-2,3-dimethylpent-4-en-1-o1, 23. The reaction was carried out according to general procedure B, using ketone **22** (0.42 g, 1.68 mmol), and reaction time was extended to 18 h. A solvent mixture of 3:1 hexanes/ethyl acetate was used for flash chromatography to give the title product (0.41 g, 95%) as a pale yellow oil. $[\alpha]_D = -0.7$ (*c* 5.5, $CHCl_3$); ν_{max}(neat)/cm^{-1} 3498 (OH), 2968 (CH), 2325, 1634, 1591, 1510, 1458, 1257, 1229, 1137, and 1025 (C−O), 902, 807 and 740; δ_H (400 MHz; $CDCl_3$) 0.53 (3H, d, *J* = 4.0 Hz, 2-CH_3), 1.01 (3H, d, *J* = 8.0 Hz, 3-CH_3), 1.89 (1H, ddq, *J* = 7.8, 8.0, 8.0 Hz, 3-H) 2.74 (1H, ddq, *J* = 4.0, 8.0, 8.0 Hz, 2-H), 3.88 (6H, s, OCH_3), 4.40 (1H, dd, *J* = 2.0, 8.0 Hz, 1-H), 5.04 (2H, m, 5-CH_2), 5.91 (1H, m, 4-H) and 6.83−6.91 (3H, m, Ar-H); δ_C (100 MHz; $CDCl_3$) 10.9 (CH_3, C-2), 13.0 (CH_3, C-3), 37.1 (CH, C-2), 44.2 (CH, C-3), 55.9 (CH_3, 2 × OCH_3), 73.9 (CH, C-1), 109.6 (CH, C-2′), 110.7 (CH, C-5′), 113.2 (CH_2, C-5), 119.3 (CH, C-6′), 136.4 (q, C-1′), 144.3 (CH and q, C-4, C-3′ and C-4′); *m*/*z* (EI) 250 (M$^+$, 10%), 167 (100), 151 (3), 139 (54), 124 (11), 108 (6), 77 (6) and 55 (8); HRMS (EI) calcd for $C_{15}H_{22}O_3$, 250.1569; found, 250.1566.

(1*R*,2*R*,3*S*)-1-(3,4-Dimethoxyphenyl)-2,3-dimethyl-1-(methoxymethoxy)pent-4-ene (MOM-23). To a stirred solution of alcohol **23** (0.12 g, 0.48 mmol) in DCM (15 mL) under an atmosphere of nitrogen at 0 °C was added diisopropylethylamine (0.34 mL, 1.9 mmol), followed by the dropwise addition of methyl methoxy chloride (0.13 mL, 1.2 mmol). The resulting solution was allowed to warm to room temperature and stirred for 24 h. Saturated NH_4Cl solution (20 mL) was added, the layers were separated, and the aqueous mixture was further extracted with DCM (3 × 30 mL). The combined organic fractions were dried ($MgSO_4$), and the solvent was removed *in vacuo*. The crude product was purified by flash chromatography (3:1 hexanes/ethyl acetate) to afford the title product (0.13 g, 91%) as a colorless oil. $[\alpha]_D = +93$ (*c* 1.56, $CHCl_3$); ν_{max}(neat)/cm^{-1} 2961 (CH), 1593 and 1516 (C═C), 1464, 1262, 1233, 1139, 1032 (C−O), 917; δ_H (400 MHz; $CDCl_3$) 0.47 (3H, d, *J* = 4.0 Hz, 2-CH_3), 0.98 (3H, d, *J* = 8.0 Hz, 3-CH_3), 1.93 (1H, m, 2-H) 2.84 (1H, m, 3-H), 3.35 (3H, s, OCH_2OCH_3), 3.85 (6H, s, 3′-OCH_3 and 4′-OCH_3), 4.31 (1H, d, *J* = 8.0 Hz, 1-H), 4.43−4.47 (2H, dd, *J* = 2.4, 8.0 Hz, OCH_2O), 5.02 (2H, m, 5-CH_2), 5.86 (1H, m, 4-H) and 6.79−6.82 (3H, m, Ar-H); δ_C (100 MHz; $CDCl_3$) 10.5 (CH_3, C-2), 11.8 (CH_3, C-3), 36.3 (CH, C-3), 43.2 (CH, C-2), 55.8 (CH_3, 3 × OCH_3), 79.9 (CH, C-1), 93.8 (CH_2, OCH_2O), 110.1 and 110.4 (CH, Ar-H), 113.1 (CH_2, C-5), 120.7 (CH, Ar-H) 133.3 (q, C-1′), 144.1 (CH, C-4), 148.4 and 148.9 (q, C-3′ and C-4′); *m*/*z* (ESI) 317 (MNa$^+$, 100%), 233 (50), 151 (71); HRMS (ESI) calcd for $C_{17}H_{26}O_4Na$, 317.1723; found, 317.1721.

(1*R*,2*R*,3*S*)-1-(3,4-Dimethoxyphenyl)-2,3-dimethyl-1-(methoxymethoxy)pentan-4,5-diol. The reaction was carried out according to general procedure C, using MOM-**23** (0.094 g, 0.32 mmol). A solvent mixture of 19:1 DCM/methanol was used for flash chromatography to give the title product as a mixture of diastereomers (0.09 g, 86%) as a pale yellow oil. ν_{max}(neat)/cm^{-1} 3413 (OH), 2936 and 2838 (CH), 1594 and 1510 (C═C), 1464, 1421, 1260, 1231, 1139, 1025 (C−O), 913 and 728; δ_H (400 MHz; $CDCl_3$) [*denotes minor diastereomer] 0.51 (3H, m, 2-CH_3), 0.84 (3H, d, *J* = 8.0 Hz, 3-CH_3), 1.01* (3H, d, *J* = 8.0 Hz, 3-CH_3), 1.91* (1H, m, 2-H), 2.24* (1H, m, 3-H), 2.32 (1H, m, 3-H), 2.41 (1H, m, 2-H), 3.34 (3H, s, OCH_2OCH_3), 3.51−3.84 (3H, m, 4-H and 5-CH_2), 3.87 (6H, s, 3′-OCH_3 and 4′-OCH_3), 4.26 (1H, m, 1-H), 4.40−4.47 (2H, dd, *J* = 20, 4.0 Hz, OCH_2O), and 6.81−6.86 (3H, m, Ar-H); δ_C (100 MHz; $CDCl_3$) 9.3* and 9.7 (CH_3,C-3), 10.3 and 11.3* (CH_3, C-2), 34.5 and 35.1* (CH, C-3), 37.9 and 40.4* (CH, C-2), 55.8 and 55.9* (CH_3, 3 × OCH_3), 65.1* and 65.5 (CH_2, C-5), 73.9 and 75.4* (CH, C-4), 80.0 and 80.3* (CH, C-1), 93.7 and 93.8* (CH_2, OCH_2O), 110.2, 110.5 and 120.7* and 120.8 (CH, Ar-H) 133.1* and 133.4 (q, C-1′), 148.5 and 149.0 (q, C-3′ and C-4′); *m*/*z* (ESI) 351 (MNa$^+$, 100%), 231 (15); HRMS (ESI) calcd for $C_{17}H_{28}NaO_6$, 351.1778; found, 351.1778.

(1*R*,2*R*,3*R*)-1-(3,4-Dimethoxyphenyl)-2,3-dimethyl-1-(methoxymethoxy)-4-butanal, 24. The reaction was carried out according to general procedure D, using (1*R*,2*R*,3*S*)-3,4-dimethoxyphenyl-2,3-dimethyl-1-(methoxymethoxy)pentan-4,5-diol (0.09 g, 0.27 mmol). A solvent mixture of 1:1 hexanes/ethyl acetate was used for flash chromatography to give the title product (0.072 g, 90%) as a pale yellow oil. $[\alpha]_D = +62$ (*c* 7.1, $CHCl_3$); ν_{max}(neat)/cm^{-1} 2938 and 2836 (CH), 1721 (C═O), 1515, 1464, 1262, 1140, 1028 (C−O), 918; δ_H (400 MHz; $CDCl_3$) 0.55 (3H, d, *J* = 8.0 Hz, 2-CH_3), 1.11 (3H, d, *J* = 8.0 Hz, 3-CH_3), 2.46 (1H, dq, *J* = 8.0, 8.0 Hz, 2-H), 2.94 (1H, ddq, *J* = 4.0, 8.0, 8.0 Hz, 3-H), 3.34 (3H, s, OCH_2OCH_3), 3.90 (6H, s, 3′-OCH_3 and 4′-OCH_3), 4.25 (1H, d, *J* = 8.0 Hz, 1-H), 4.40−4.48 (2H, m, OCH_2O), 6.83−6.84 (3H, m, Ar-H) and 9.70 (1H, s, 4-H); δ_C (100 MHz; $CDCl_3$) 8.0 (CH_3, C-3), 12.2 (CH_3, C-2), 38.8 (CH, C-2), 47.7 (CH, C-3), 55.9, 55.9, and 56.1 (CH_3, 3 × OCH_3), 80.1 (CH, C-1), 93.8 (CH_2, OCH_2O), 110.0 and 110.7 and 120.8 (CH, Ar-H) 132.4 (q, C-1′), 148.8 and 149.2 (q, C-3′ and C-4′) and 205.1 (C═O, C-4); *m*/*z* (ESI) 319 (MNa$^+$, 100%), 235 (29), 151 (5); HRMS (ESI) calcd for $C_{16}H_{24}NaO_5$, 319.1516; found, 319.1519

(1*R*,2*R*,3*S*,4*S*)-1,4-Bis(3,4-dimethoxyphenyl)-2,3-dimethyl-1-(methoxymethoxy)butan-4-o1, 25. The reaction was carried out according to general procedure A, using bromide **21** (0.053 g, 0.20 mmol) and *tert*-butyllithium (0.27 mL, 0.41 mmol, 1.5 M in pentane) with aldehyde **24** (0.05 g, 0.17 mmol). A solvent mixture of 2:1 ethyl acetate/hexanes was used for flash chromatography to give the

title product (0.052 g, 71%) as a yellow oil. $[\alpha]_D$ = +54 (*c* 2.0, $CHCl_3$); ν_{max}(neat)/cm^{-1} 3424 (OH), 2936 and 2837 (CH), 1731, 1703, 1594 and 1514, 1463, 1421, 1262, 1139, 1032 (C−O); δ_H (400 MHz; $CDCl_3$) 0.53 (3H, d, *J* = 4.0 Hz, 2-CH_3), 1.09 (3H, d, *J* = 4.0 Hz, 3-CH_3) 1.68 (1H, m, 2-H), 1.84 (1H, br s, OH), 2.51 (1H, m, 3-H), 3.37 (3H, s, OCH_2OCH_3), 3.79 and 3.88 (12H, s, OCH_3), 4.26 (1H, d, *J* = 12.0 Hz, 1-H), 4.39 −4.47 (2H, m, OCH_2O), 4.48 (1H, d, *J* = 4.0 Hz, 4-H), 6.62−6.91 (6H, m, Ar-H). δ_C (100 MHz; $CDCl_3$) 10.1 (CH_3, C-3), 11.4 (CH_3, C-2), 39.0 (CH, C-3), 40.0 (CH, C-2), 55.8 and 55.9 (4 × CH_3, OCH_3), 78.3 (CH, C-4), 80.5 (CH, C-1), 94.0 (CH_2, OCH_2O), 109.6, 110.2, 110.5, and 110.8 (CH, C-2′, C-2″, C-5′ and C-5″), 119.2 and 120.3 (CH, C-6′ and C-6″), 133.4 and 136.3 (q, C-1′ and C-1″), 148.3, 148.4, 148.8, and 149.0 (q, C-3′, C-3″, C-4′ and C-4″); *m*/*z* (ESI) 435 (MH^+, 90%), 426 (100); HRMS (ESI) calcd for $C_{24}H_{35}O_7$, 435.2377; found, 435.2398.

(+)-Galbelgin, (+)-1. The reaction was carried out according to general procedure E, using alcohol **25** (68 mg, 0.15 mmol) and extending the reaction time to 16 h. A solvent mixture of 4:1 hexanes/ethyl acetate was used for flash chromatography to give the title product (34 mg, 59%) as white solid. $[\alpha]_D$ = +81.8 (*c* 1.5, $CHCl_3$) [lit.[2a] $[\alpha]_D$ = +80.7 (*c* 0.55, $CHCl_3$)]; δ_H (400 MHz; $CDCl_3$) 1.05 (6H, d, *J* = 8.0 Hz, 3-CH_3 and 4-CH_3), 1.80 (2H, m, 3-H and 4-H) 3.88 and 3.92 (12H, s, all OCH_3), 4.66 (2H, d, *J* = 8.0 Hz, 2-H and 5-H), 6.85 (2H, d, *J* = 8.0 Hz, 5′-H and 5″-H), 6.91 (2H, dd, *J* = 4.0, 8.0 Hz, 6′-H and 6″-H) and 6.97 (2H, d, *J* = 4.0 Hz, 2′-H and 2″-H). δ_C (100 MHz; $CDCl_3$) 13.9 (CH_3, C-3 and C-4), 51.0 (CH, C-3 and C-4), 55.9 and 55.9 (CH_3, 4 × OCH_3), 88.3 (CH, C-2 and C-5), 109.2 and 110.8 (CH, C-2′, C-2″, C-6′ and C-6″), 118.6 (CH, C-5′ and C-5″) 134.9 (q, C-1′), 148.5 and 149.1 (q, C-3′ and C-3″ and C-4′ and C-4″). The ^{1}H and ^{13}C NMR spectra were in agreement with literature values.[2a]

(2*R,3*S**)-1-(4-Methoxyphenyl)-2,3-dimethylpent-4-en-1-one.** To a solution of 4-bromoanisole (0.76 g, 4 mmol) in THF (10 mL) under an atmosphere of nitrogen at −78 °C was added *n*-butyllithium (2.75 mL, 4.4 mmol, 1.6 M in *n*-hexanes), and the resultant solution was stirred for 5 min. A solution of (2*R**,3*S**)-2,3-dimethyl-1-morpholino-pent-4-en-1-one[9] (0.66 g, 3.4 mmol) in THF (10 mL) was then added dropwise, and the mixture was stirred at room temperature for 1.5 h. Saturated NH_4Cl solution (20 mL) was added, and the aqueous mixture was extracted with ethyl acetate (3 × 20 mL). The combined organic extracts were washed with brine (30 mL) and dried ($MgSO_4$), and the solvent was removed *in vacuo*. The crude product was purified by flash chromatography (3:1 hexanes/ethyl acetate) to give the title product (0.71 g, 96%) as a pale yellow oil. ν_{max}(neat)/cm^{-1} 3077 and 3069 (CH), 1672 (C═O), 1600 (C═C), 1509, 1256, and 1171 (C−O) and 1031 (CH); δ_H (400 MHz; $CDCl_3$) 1.00 (3H, d, *J* = 8.0 Hz, 3-CH_3), 1.13 (3H, d, *J* = 4.0 Hz, 2-CH_3), 2.64 (1H, m, 3-H), 3.42 (1H, m, 2-H), 3.87 (3H, s, OCH_3), 4.92−5.02 (2H, m, 5-CH_2), 5.81 (1H, m, 4-H), 6.94 (2H, d, *J* = 8.0 Hz, 3′-H) and 7.91 (2H, d, *J* = 8.0 Hz, 2′-H); δ_C (75 MHz; $CDCl_3$) 13.3 (CH_3, C-2), 15.5 (CH_3, C-3), 39.9 (CH, C-3), 44.8 (CH, C-2), 55.4 (CH_3, OCH_3), 113.7 (CH, C-3′), 113.9 (CH_2, C-5), 130.3 (q, C-1′), 130.5 (CH, C-2′), 142.2 (CH, C-4), 163.3 (CH, C-4′) and 202.3 (q, C-1); *m*/*z* (CI) 219 (MH^+, 75%), 203 (8), 162 (11),135 (100), 121 (10), 111 (14), 97 (12), 84 (14), 70 (17); HRMS (CI) calcd for $C_{14}H_{19}O_2$, 219.1385; found, 219.1392.

(1*R,2*R**,3*S**)-1-(4-Methoxyphenyl)-2,3-dimethylpent-4-en-1-ol, 32.** The reaction was carried out according to general procedure B, using (2*R**,3*S**)-1-(4-methoxyphenyl)-2,3-dimethylpent-4-en-1-one (0.74 g, 3.4 mmol). A solvent mixture of 4:1 hexanes/ethyl acetate was used for flash chromatography to give the title product (0.65 g, 86%) as a pale yellow oil. ν_{max}(neat)/cm^{-1} 3407 (OH), 3079 (CH), 2965, 2818, 1612 (C═C alkene), 1586 (C═C aromatic), 1462, 1377 and 1301, 1249, 1175, and 1036 (C−O), 832; δ_H (400 MHz; $CDCl_3$) 0.52 (3H, d, *J* = 8.0 Hz, 3-CH_3), 1.00 (3H, d, *J* = 4.0 Hz, 2-CH_3), 1.90 (1H, m, 3-H), 2.72 (1H, m, 2-H), 3.81 (3H, s, OCH_3), 4.42 (1H, m, 1-H), 5.04 (2H, m, 5-CH_2), 5.89 (1H, m, 4-H), 6.87 (2H, d, *J* = 8.0 Hz, 3′-H), 7.25 (2H, d, *J* = 8.0 Hz, 2′-H); δ_C (100 MHz; $CDCl_3$) 10.9 (CH_3, C-2), 12.9 (CH_3, C-3), 37.0 (CH, C-3), 44.2 (CH, C-2), 55.3 (CH_3, OCH_3), 76.6 (CH, C-1), 113.2 (CH_2, C-5), 113.7 (CH, C-3′), 128.0 (CH, C-2′), 133.0 (q, C-1′), 144.3 (CH, C-4), 159.1 (q, C-4′); *m*/*z* (EI) 220 (M^+, 4%), 137 (100), 135 (3), 109 (8), 94 (5), 77 (7), 55 (4), 39 (3); HRMS (EI) calcd for $C_{14}H_{20}O_2$, 220.1463; found, 220.1466.

(1*R,2*R**,3*S**)-1-(4-Methoxyphenyl)-2,3-dimethyl-1-(*tert*-butyldimethylsiloxy)pent-4-ene, 33.** To a stirred solution of alcohol **32** (0.1 g, 0.45 mmol) in DCM (5 mL) was added imidazole (0.12 g, 1.8 mmol). The mixture was cooled to 0 °C, and TBS chloride (0.081 g, 0.54 mmol) was added. The resulting solution stirred under an atmosphere of nitrogen at room temperature for 48 h. Water (5 mL) was added, the layers were separated, the aqueous mixture was further extracted with ethyl acetate (3 × 20 mL) and then dried ($MgSO_4$), and the solvent was removed *in vacuo*. The crude product was purified by flash chromatography (9:1 hexanes/ethyl acetate) to afford the title product (0.14 g, 87%) as a colorless oil. ν_{max}(neat)/cm^{-1} 2957 and 2855 (CH), 2346 (CH), 1612 and 1512 (C═C), 1462 1299, 1250, 1172, 1073, and 1035 (C−O), 909, 835, and 775 (CH); δ_H (300 MHz; $CDCl_3$) −0.33 and −0.01 (2 × 3H, s, Si-CH_3), 0.47 (3H, d, *J* = 6.0 Hz, 2-CH_3), 0.83 (9H, s, $SiC(CH_3)_3$), 0.91 (3H, d, *J* = 9.0 Hz, 3-CH_3), 1.77 (1H, m, 2-H) 2.70 (1H, m, 3-H), 3.79 (3H, s, OCH_3), 4.34 (1H, d, *J* = 9.0 Hz, 1-H), 4.99 (2H, m, 5-CH_2), 5.84 (1H, m, 4-H), 6.81 (2H, d, *J* = 9.0 Hz, 3′-H), 7.21 (2H, d, *J* = 9.0 Hz, 2′-H); δ_C (75 MHz; $CDCl_3$) −5.2 and −4.5 (2 × CH_3, $SiCH_3$), 10.3 (CH_3, C-2), 12.5 (CH_3, C-3), 18.1 (q, $C(CH_3)_3$), 25.8 (CH_3, $C(CH_3)_3$), 36.2 (CH, C-3), 45.6 (CH, C-2), 55.1 (CH_3, OCH_3), 77.0 (CH, C-1), 112.7 (CH_2, C-5), 113.1 (2 × CH, C-3′), 128.2 (2 × CH, C-2′), 136.4 (q, C-1), 144.9 (CH, C-4) and 158.6 (q, C-4′) ; *m*/*z* (CI): 335 (MH^+, 1%), 277 (6), 251 (100), 202 (10), 93 (4), 187 (7), 135 (3), 121 (19), 73 (21), 70 (21); HRMS (CI) calcd for $C_{20}H_{35}O_2Si$, 335.2406; found, 335.2416.

(1*R,2*R**,3*R**)-1-(4-Methoxyphenyl)-2,3-dimethyl-1-(*tert*-butyldimethylsiloxy)pentan-4,5-diol.** The reaction was carried out according to general procedure C, using alkene **33** (0.135 g, 0.4 mmol). A solvent mixture of 14:1 DCM/methanol was used for flash chromatography to give the title product (0.12 g, 81%) as a colorless oil. ν_{max}(film)/cm^{-1} 3387 (OH), 2956 and 2928 (CH), 2856 (CH), 1611 and 1512 (C═C), 1249, 1173, 1069, and 1039 (C−O), 864 835 and 775; δ_H (400 MHz; $CDCl_3$) [*denotes minor diastereomer] −0.35*, −0.34, −0.02* and −0.01 (2 × 3H, s, Si-CH_3), 0.54 (3H, d, *J* = 8.0 Hz, 2-CH_3), 0.79 (3H, d, *J* = 8.0 Hz, 3-CH_3), 0.83 (9H, s, $SiC(CH_3)_3$), 0.89−0.93* (6H, m, 2-CH_3 and 3-CH_3), 1.72 (2H, br s, 4-OH and 5-OH) 2.14−2.17 (2H, m, 2-H and 3-H), 3.45−3.74 (3H, m, 4-H and 5-CH_2), 3.79 (3H, s, OCH_3), 4.26 (1H, d, *J* = 12.0 Hz, 1-H), 6.82 (2H, d, *J* = 8.0 Hz, 3′-H), 7.17 (2H, d, *J* = 8.0 Hz, 2′-H); δ_C (100 MHz; $CDCl_3$) −5.2 and −4.4 (2 × CH_3, Si-CH_3), 9.6* and 10.3 (CH_3, C-3), 10.7 and 11.4* (CH_3, C-2), 18.1 (q, $C(CH_3)_3$), 25.8 (CH_3, $C(CH_3)_3$), 34.5, 34.8*, 40.4 and 42.7* (CH, C-2 and C-3), 55.2 (CH_3, OCH_3), 65.6* and 65.7 (CH_2, C-5), 74.5 (CH, C-4), 77.7 (CH, C-1), 113.3 (CH, C-3′), 128.1 (CH, C-2′), 136.6 (q, C-1′) and 158.7 (CH, C-4′); *m*/*z* (FAB): 369 (MH^+, 3%), 251 (96), 237 (23), 201 (22), 121 (42), 89 (18) and 73 (100); HRMS (CI/NH_3) calcd for $C_{16}H_{30}NO_5$, 316.2124.; found, 316.2119.

(1*R,2*R**,3*R**)-1-(4-Methoxyphenyl)-2,3-dimethyl-1-(*tert*-butyldimethylsiloxy)-4-butanal, 34.** The reaction was carried out according to general procedure D, using (1*R**,2*R**,3*R**)-4-methoxyphenyl-2,3-dimethyl-1-(*tert*-butyldimethylsiloxy)pentan-4,5-diol (1.13 g, 3.1 mmol) extending the reaction time to 6 h. A solvent mixture of 2:1 hexanes/ethyl acetate was used for flash chromatography to give the title product (0.88 g, 85%) as a colorless oil. ν_{max}(film)/cm^{-1} 2956 and 2930 (CH), 1721 (C═O), 1612 and 1511 (C═C), 1248, 1173, and 1066 (C−O), 906, 860, 835 and 728; δ_H (300 MHz; $CDCl_3$) −0.34 and −0.03 (2 × 3H, s, $SiCH_3$), 0.50 (3H, d, *J* = 9.0 Hz, 2-CH_3), 0.82 (9H, s,

$SiC(CH_3)_3$), 1.03 (3H, d, J = 6.0 Hz, 3-CH_3), 2.35 (1H, m, 3-H), 2.91 (1H, dq, J = 8.1, 8.9 Hz, 2-H), 3.78 (3H, s, OCH_3), 4.29 (1H, d, J = 9.0, 1-H), 6.82 (2H, d, J = 9.0 Hz, 3′-H), 7.18 (2H, d, J = 9.0 Hz, 2′-H); δ_C (75 MHz; $CDCl_3$) −5.2 and −4.5 (2 × CH_3, Si-CH_3), 7.4 (CH_3, C-3), 11.6 (CH_3, C-2), 18.0 (q, $C(CH_3)_3$), 25.8 (CH_3, $C(CH_3)_3$), 40.6 (CH, C-3), 47.0 (CH, C-2), 55.1 (CH_3, OCH_3), 77.2 (CH, C-1), 113.4 (CH, C-3′), 128.1 (CH, C-2′), 135.6 (q, C-1′) 159.0 (q, C-4′) and 205.6 (C═O, C-4); m/z (CI) 337 (MH^+, 24%), 279 (70), 251 (81), 205 (100), 187 (31), 175 (19), 121 (50), 75 (68) and 73 (42); HRMS (CI) calcd for $C_{19}H_{33}O_3Si$, 337.2199; found, 337.2197.

(1*R,2*R**,3*S**,4*S**)-1,4-Bis(4-methoxyphenyl)-2,3-dimethyl-1-(*tert*-butyldimethylsiloxy)butan-4-o1, 35.** To a solution of 4-bromoanisole (0.53 g, 2.9 mmol) in THF (5 mL) under an atmosphere of nitrogen at −78 °C was added *n*-butyllithium (1.9 mL, 2.9 mmol, 1.5 M in hexanes), and the resultant solution was stirred for 5 min. A solution of aldehyde **34** (0.8 g, 2.4 mmol) in THF (5 mL) was then added dropwise, and the mixture was stirred at room temperature for 18 h. Saturated NH_4Cl solution (10 mL) was added, and the aqueous mixture was extracted with ethyl acetate (3 × 10 mL). The combined organic extracts were washed with brine (10 mL) and dried ($MgSO_4$), and the solvent was removed *in vacuo*. The crude product was purified by flash chromatography (4:1 hexanes/ethyl acetate) to give the title product (0.97 g, 92%) as a colorless oil. ν_{max}(film)/cm^{-1} 3458 (OH), 2955, 2928 2855, 1611, 1510 (C═C), 1462, 1379, 1302, 1246, 1173, 1064, 1035, and 1005 (C−O), 863, 831 and 774; δ_H (300 MHz; $CDCl_3$) −0.38 and −0.01 (2 × 3H, s, Si-CH_3), 0.48 (3H, d, J = 9.0 Hz, 2-CH_3), 0.86 (9H, s, $SiC(CH_3)_3$), 1.03 (3H, d, J = 6.0 Hz, 3-CH_3), 1.50 (1H, m, 3-H), 1.72 (1H, br s, OH) 2.46 (1H, m, 2-H), 3.77 and 3.81 (2x 3H, s, OCH_3), 4.24 (1H, d, J = 9.0 Hz, 1-H), 4.39 (1H, d, J = 9.0 Hz, 4-H), 6.75 (2H, d, J = 9.0 Hz, 3′-H or 3″-H), 6.85 (2H, d, J = 9.0 Hz, 3′-H or 3″-H), 6.99 (2H, d, J = 6.0 Hz, 2′-H or 2″-H) and 7.20 (2H, d, J = 6.0 Hz, 2′-H or 2″-H); δ_C (100 MHz; $CDCl_3$) −5.2 and −4.5 (2x CH_3, Si-CH_3), 10.1 (CH_3, C-3), 10.9 (CH_3, C-2), 18.0 (q, $C(CH_3)_3$), 25.8 (CH_3, $C(CH_3)_3$), 38.3 (CH, C-2), 41.7 (CH, C-3), 55.1 and 55.2 (CH_3, OCH_3), 77.5 (CH, C-1), 78.2 (CH, C-4), 113.1 and 113.7 (CH, C-3′ and C-3″), 127.9 (CH, C-2′ and C-2″), 135.9 and 136.5 (q, C-1′ and C-1″), 158.5 and 158.9 (q, C-4′ and C-4″); m/z (FAB) 427 (M − OH^+, 10%), 295 (23), 251 (77), 121 (48) and 73 (100); HRMS (FAB) calcd for $C_{26}H_{39}O_3Si$, 427.2669; found, 427.26703.

(2*R,3*R**)-4,4-Bis(4-methoxyphenyl)-2,3-dimethylbutanal, 36.** The reaction was carried out according to general procedure E, using alcohol **35** (0.052 g, 0.12 mmol) and extending the reaction time to 7 h. A solvent mixture of 9:1 hexanes/ethyl acetate was used for flash chromatography to give the title product (30.6 mg, 85%) as a colorless oil. ν_{max}(film)/cm^{-1} 2961, 2833, 1718 (C═O), 1605, 1507, 1461, 1299, 1243, 1173, and 1032 (C−O), 814, 747, 666; δ_H (300 MHz; $CDCl_3$) 0.70 (3H, d, J = 6.0 Hz, 2-CH_3), 1.01 (3H, d, J = 6.0 Hz, 3-CH_3), 2.38 (1H, m, 3-H), 3.02 (1H, m, 2-H), 3.59 (1H, d, J = 12.0 Hz, 1-H), 3.75 (6H, s, OCH_3), 6.82 (4H, d, J = 9.0 Hz, 3′-H and 3″-H), 7.23 (4H, d, J = 9.0 Hz, 2′-H and 2″-H) and 9.64 (1H, s, 4-H); δ_C (100 MHz; $CDCl_3$) 6.2 (CH_3, C-3), 13.6 (CH_3, C-2), 35.6 (CH, C-2), 47.9 (CH, C-3), 54.6 (CH, C-1), 55.2 (CH_3, OCH_3), 114.0 and 114.3 (CH, C-3′ and C-3″), 128.5 and 128.6 (CH, C-2′ and C-2″), 135.9 (q, C-1′ and C-1″), 158.0 and 158.1 (q, OCH_3), 205.4 (C═O, C-4); m/z (EI) 312 (M^+, 5%), 254 (8), 227 (100), 176 (6) and 115 (4); HRMS (EI) calcd for $C_{20}H_{24}O_3$, 312.1725; found, 312.1723.

(2*R,3*R**)-4,4-Bis(4-methoxyphenyl)-2,3-dimethylbutanol, 39.** The reaction was carried out according to general procedure B, using aldehyde **36** (0.017 g, 0.05 mmol) and reducing the reaction time to 3 1/2 h. A solvent mixture of 4:1 hexanes/ethyl acetate was used for flash chromatography to give the title product (11.7 mg, 64%) as a pale yellow oil. ν_{max}(film)/cm^{-1} 3399 (OH), 2961 and 2833 (CH), 1605, 1507, 1461, 1243, 1176, 1032, 817, 564; δ_H (400 MHz; $CDCl_3$) 0.67 (3H, d, J = 4.0 Hz, 2-CH_3), 0.75 (3H, d, J = 8.0 Hz, 3-CH_3), 1.73 (1H, m, 3-H), 2.61 (1H, m, 2-H), 3.45−3.50 (2H, m, 4-CH_2), 3.55 (1H, d, J = 12.0 Hz, 1-H), 3.76 (6H, s, 2 × OCH_3), 6.79−6.81 (4H, m, 3′-H and 3″-H), 7.19−7.22 (4H, m, 2′-H and 2″-H); δ_C (75 MHz; $CDCl_3$) 9.4 (CH_3, C-3), 11.8 (CH_3, C-2), 36.0 (CH, C-2), 55.0 (CH, C-3), 55.1 (2 × CH_3, OCH_3), 67.1 (CH_2, CH_2OH), 113.8 and 114.0 (CH, C-3′ and C-3″), 128.6 and 128.7 (CH, C-2′ and C-2″), 136.8 and 137.3 (q, C-1′ and C-1″), 157.7 and 157.7 (q, C-4′ and C-4″); m/z (EI) 314 (M^+, 8%), 227 (100), 212 (4), 121 (4), 115 (5); HRMS (EI) calcd for $C_{20}H_{26}O_3$, 314.1882; found, 314.1882.

(1*R*,2*R*,3*S*)-1-(3,4-Dimethoxyphenyl)-2,3-dimethyl-1-(*tert*-butyldimethylsiloxy)pent-4-ene, 40. To a stirred solution of alcohol **23** (0.32 g, 1.3 mmol) in DCM (10 mL) was added imidazole (0.36 g, 5.2 mmol). The mixture was cooled to 0 °C, and TBS chloride (0.24 g, 1.6 mmol) was added. The resulting solution stirred under an atmosphere of nitrogen at room temperature for 14 days. Water (10 mL) was added, the layers were separated, the aqueous mixture was further extracted with ethyl acetate (3 × 20 mL) and then dried ($MgSO_4$), and the solvent was removed *in vacuo*. The crude product was purified by flash chromatography (4:1 hexanes/ethyl acetate) to afford the title product (0.33 g, 72%) as a colorless oil. $[\alpha]_D$ = +23.0 (*c* 3.1, $CHCl_3$); ν_{max}(neat)/cm^{-1} 2956 and 2857 (CH), 1514, 1463 (C═C), 1259, 1140, 1073, 1031 (C−O), 861, 835, 775 and 669; δ_H (400 MHz; $CDCl_3$) −0.30 and −0.00 (2 × 3H, s, Si-CH_3), 0.48 (3H, d, J = 4.0 Hz, 2-CH_3), 0.84 (9H, s, $SiC(CH_3)_3$), 0.92 (3H, d, J = 8.0 Hz, 3-CH_3), 1.76 (1H, m, 2-H) 2.71 (1H, m, 3-H), 3.86 (3H, s, 2 × OCH_3), 4.34 (1H, d, J = 8.0 Hz, 1-H), 5.01 (2H, m, 5-CH_2), 5.85 (1H, m, 4-H), 6.75 (2H, s, 5′-CH and 6′-CH) and 6.86 (1H, s, 2′-H); δ_C (100 MHz; $CDCl_3$) −5.1 and −4.5 (2 × CH_3, $SiCH_3$), 10.3 (CH_3,C-2), 12.5 (CH_3, C-3), 18.1 (q, $C(CH_3)_3$), 25.8 (CH_3, $C(CH_3)_3$), 36.2 (CH, C-3), 45.6 (CH, C-2), 55.8 (CH_3, 2 × OCH_3), 77.2 (CH, C-1), 110.0 (CH, C-2′), 110.1 (CH, C-5′ or C-6′), 112.8 (CH_2, C-5), 119.5 (CH, C-5′ or C-6′), 136.9 (q, C-1′), 144.8 (CH, C-4), 148.0 and 148.6 (q, C-3′ and C-4′); m/z (EI) 364 (M^+, 2%), 307 (5), 281 (100), 151 (14), 73 (29) and 55 (4), HRMS (EI) calcd for $C_{21}H_{36}O_3Si$, 364.2434; found, 364.2433.

(1*R*,2*R*,3*S*)-1-(3,4-Dimethoxyphenyl)-2,3-dimethyl-1-(*tert*-butyldimethylsiloxy)pentan-4,5-diol. The reaction was carried out according to general procedure C, using alkene **40** (0.33 g, 0.9 mmol). A solvent mixture of 19:1 DCM/methanol was used for flash chromatography to give the title product (0.34 g, 94%) as a pale yellow oil. ν_{max}(neat)/cm^{-1} 3412 (OH), 2930, 2856, 1593, 1513 (C═C), 1463, 1259, 1139, 1069, and 1030 (C−O), 861, 835 and 774; δ_H (300 MHz; $CDCl_3$) [*denotes minor diastereomer] −0.31 and −0.01 (2 × 3H, s, $SiCH_3$), 0.55 (3H, d, J = 6.0 Hz, 2-CH_3), 0.79 (3H, d, J = 6.0 Hz, 3-CH_3), 0.84 (9H, s, $C(CH_3)_3$), 0.88−0.91* (6H, m, 2-CH_3 and 3-CH_3), 1.89−2.18 (4H, m, 2-H, 3-H and 2 × OH), 3.46−3.76 (3H, m, 4-H and 5-CH_2), 3.86 (6H, s, 2 × OCH_3), 4.25 (1H, d, J = 9.0 Hz, 1-H), 6.74−6.85 (3H, m, Ar-H); δ_C (100 MHz; $CDCl_3$) −5.2 and −4.5 (2 × CH_3, $SiCH_3$), 9.6* and 10.3 (CH_3, C-3), 10.7 and 11.5* (CH_3, C-2), 18.1 (q, $C(CH_3)_3$), 25.8 (CH_3, $C(CH_3)_3$), 34.5 and 34.5* (CH, C-3), 40.3 and 42.7* (CH, C-2), 55.8 (CH_3, 2 × OCH_3), 65.6* and 65.7 (CH_2, C-5), 74.4 and 76.2* (CH, C-4), 77.9 (CH, C-1), 109.7 (CH, C-2′), 110.2 and 110.2* (CH, C-5′), 119.4 and 119.4* (CH, C-6′), 136.8* and 137.1 (q, C-1′) and 148.1* and 148.7 (2q, C-3′ and C-4′); m/z (EI) 398 (M^+, 1%), 281 (100), 235 (11), 166 (17), 151 (21), 73 (69) and 71 (26); HRMS (EI) calcd for $C_{21}H_{38}O_5Si$, 398.2489; found, 398.2486.

(1*R*,2*R*,3*R*)-1-(3,4-Dimethoxyphenyl)-2,3-dimethyl-1-(*tert*-butyldimethylsiloxy)-4-butanal, 41. The reaction was carried out according to general procedure D, using (1*R*,2*R*,3*S*)-3,4-dimethoxyphenyl-2,3-dimethyl-1-(*tert*-butyldimethylsiloxy)pentan-4,5-diol (0.34 g, 0.85 mmol). A solvent mixture of 9:1 hexanes/ethyl acetate was used for flash chromatography to give the title product (0.28 g, 90%) as a pale yellow oil. $[\alpha]_D$ = −10.0 (*c* 4.15, $CHCl_3$); ν_{max}(neat)/cm^{-1} 2955, 2931, and 2857 (CH), 1723 (C═O), 1594 and 1515 (C═C), 1463, 1259,

1142, and 1066 (C−O), 1030, 860, 836, 776; δ_H (400 MHz; $CDCl_3$) −0.29 and −0.00 (2 × 3H, s, $SiCH_3$), 0.53 (3H, d, J = 4.0 Hz, 2-CH_3), 0.85 (9H, s, $C(CH_3)_3$), 1.05 (3H, d, J = 8.0 Hz, 3-CH_3), 2.36 (1H, m, 3-H), 2.92 (1H, m, 2-H), 3.88 (6H, s, 2 × OCH_3), 4.30 (1H, d, J = 12.0 Hz, 1-H), 6.77−6.78 (2H, m, 5′-H and 2′-H or 6′-H), 6.88 (1H, d, J = 1.5 Hz, 2′-H or 6′-H) and 9.66 (1H, s, 4-H); δ_C (100 MHz; $CDCl_3$) −5.2 and −4.5 (2 × CH_3, $SiCH_3$), 7.4 (CH_3, C-3), 11.7 (CH_3, C-2), 18.1 (q, $C(CH_3)_3$), 25.8 (CH_3, $C(CH_3)_3$), 40.5 (CH, C-3), 47.0 (CH, C-2), 55.8 (2 × CH_3, OCH_3), 77.4 (CH, C-1), 109.6 (CH, C-2′ or C-6′), 110.3 (CH, C-5′), 119.5 (CH, C-2′ or C-6′), 136.0 (q, C-1′), 148.3 and 148.8 (q, C-3′ and C-4′) and 205.7 (C=O, C-4); m/z (EI) 366 (M^+, 2%), 309 (42), 281 (98), 234 (11), 151 (26), 83 (22), 73 (100) and 71 (49); HRMS (EI) calcd for $C_{20}H_{34}O_4Si$, 366.2226; found, 366.2224.

(1*R*,2*R*,3*S*,4*S*)-1,4-Bis(3,4-dimethoxyphenyl)-2,3-dimethyl-1-(*tert*-butyldimethylsiloxy)butan-4-o1, 42. The reaction was carried out according to general procedure A, using bromide **21** (0.14 g, 0.66 mmol) and *tert*-butyllithium (0.87 mL, 1.3 mmol, 1.5 M) with aldehyde **41** (0.2 g, 0.55 mmol). A solvent mixture of 4:1 hexanes/ethyl acetate was used for flash chromatography to give the title product (0.15 g, 54%) as a pale yellow oil. $[\alpha]_D$ = +65.0 (c 4.1, $CHCl_3$); ν_{max}(neat)/cm^{-1} 3541, 2955, and 2853 (CH), 1594 and 1512 (C=C), 1464, 1418, 1261, 1138, and 1029 (C−O), 859, 836, 776; δ_H (300 MHz; $CDCl_3$) −0.34 and −0.00 (2 × 3H, s, $SiCH_3$), 0.56 (3H, d, J = 9.0 Hz, 3-CH_3), 0.86 (9H, s, $C(CH_3)_3$), 1.04 (3H, d, J = 6.0 Hz, 2-CH_3), 1.48 (1H, m, 3-H), 1.62 (1H, br s, 4-OH), 2.38 (1H, m, 2-H), 3.83 and 3.86 (each 6H, s, OCH_3), 4.26 (1H, d, J = 6.0 Hz, 4-H), 4.37 (1H, d, J = 9.0 Hz, 1-H) and 6.61−6.80 (6H, m, Ar-H); δ_C (75 MHz; $CDCl_3$) −5.2 and −4.5 (2 × CH_3, $SiCH_3$), 10.2 (CH_3, C-2), 11.2 (CH_3, C-3), 18.1 (q, $C(CH_3)_3$), 25.9 (CH_3, $C(CH_3)_3$), 38.4 (CH, C-2), 41.8 (CH, C-3), 55.7, 55.7, 55.8, and 55.9 (4 × CH_3, OCH_3), 78.0 (CH, C-4), 78.7 (CH, C-1), 109.2, 109.8, 110.2, and 110.6 (4 × CH, C-2′ and C-5′ and C-3″ and C-6″), 119.1 and 119.3 (2 × CH, C-2″ and C-6′), 136.5 and 137.1 (2q, C-1′ and C-1″), 147.9, 148.4, and 149.1 (4q, C-3′ and C-4′ and C-4″ and C-5″); m/z (EI) 504 (M^+, 2%), 354 (77), 281 (86) and 73 (100); HRMS (EI) calcd for $C_{28}H_{44}O_6Si$, 504.2907; found, 504.2910.

Cyclogalgravin, (−)-3. The reaction was carried out according to general procedure E, using alcohol **42** (0.028 g, 0.056 mmol) and extending the reaction time to 16 h. A solvent mixture of 4:1 hexanes/ethyl acetate was used for flash chromatography to give the title product (19 mg, 95%) as a colorless oil that solidified upon standing. $[\alpha]_D$ = −128.0 (c 0.2, $CHCl_3$) [lit.[17] $[\alpha]_D$ = −105.9 (c 1.07, $CHCl_3$) lit. ent[4b] $[\alpha]_D$ = +135.5 (c 0.25, $CHCl_3$)]; ν_{max}(neat)/cm^{-1} 2996 and 2957, 2833, 1604, 1509 (C=C), 1463, 1262, 1229, 1141, 1120, 1028 (C−O), 869 and 759; δ_H (300 MHz; $CDCl_3$) 1.08 (3H, d, J = 9.0 Hz, 9′-CH_3), 1.79 (3H, d, J = 3.0 Hz, 9-CH_3), 2.40 (1H, m, 8′-H), 3.67 (1H, d, J = 3.0 Hz, 7′-H), 3.78 (6H, s, OCH_3), 3.82 (3H, s, OCH_3), 3.88 (3H, s, OCH_3), 6.14 (1H, s, 7-H), 6.54−6.57 (2H, m, 3-H and 6′-H), 6.62 (1H, s, 6-H), 6.66 (1H, d, J = 3.0 Hz, 2′-H) and 6.72 (1H, d, J = 9.0 Hz, 5′-H); δ_C (75 MHz; $CDCl_3$) 18.6 (CH_3, C-9′), 22.1 (CH_3, C-9), 42.0 (CH, C-8′), 50.8 (CH, C-7′), 55.7, 55.8, 55.9 (4 × CH_3, OCH_3), 108.9 (CH, C-6), 110.9 (CH, C-5′), 111.0 (CH, C-2′), 112.8 (CH, C-3), 119.6 (CH, C-6′), 121.1 (CH, C-7), 127.1 (q, C-1), 127.3 (q, C-2), 138.1 (q, C-1′), 138.8 (q, C-8), 147.3 (q, C-4′), 147.5 (q, C-4), 147.6 (q, C-5), 148.6 (q, C-3′); m/z (ESI) 377 (MNa^+, 100%), 372 (8), 355 (MH+, 12); HRMS (ESI) calcd for $C_{22}H_{27}O_4$, 355.1904; found, 355.1904. All spectral data were in agreement with the literature values.[4b]

(1*R*,2*R*,3*S*,4*S*)-1-(3,4-Dimethoxyphenyl)-2,3-dimethyl-4-(4-methoxymethoxyphenyl)-1-(*tert*-butyldimethylsiloxy)butan-4-o1, 47. The reaction was carried out according to general procedure A, using 1-bromo-4-(methoxymethoxy)benzene (0.1 g, 0.47 mmol) and *tert*-butyllithium (0.63 mL, 0.95 mmol, 1.5 M) with aldehyde **41** (0.15 g, 0.40 mmol). A solvent mixture of 3:1 hexanes/ethyl acetate was used for flash chromatography to give the title product (0.12 g, 60%) as a yellow oil. $[\alpha]_D$ = +53 (c 1.0, $CHCl_3$); ν_{max}(neat)/cm^{-1} 3509 (OH), 2956, 2930, and 2856 (CH), 1609, 1509 (C=C), 1463, 1256, 1230, 1151, 1073, and 1004 (C−O) and 833; δ_H (400 MHz; $CDCl_3$) −0.34 and −0.01 (2 × 3H, s, $SiCH_3$), 0.54 (3H, d, J = 7.2 Hz, 2-CH_3), 0.87 (9H, s, $C(CH_3)_3$), 1.02 (3H, d, J = 6.8 Hz, 3-CH_3), 1.49 (1H, m, 2-H), 2.39 (1H, m, 3-H), 3.46 (3H, s, OCH_2OCH_3), 3.76 and 3.84 (2 × CH_3, s, OCH_3), 4.24 (1H, d, J = 7.6 Hz, 1-H), 4.37 (1H, d, J = 8.8 Hz, 4-H), 5.15 (2H, s, OCH_2O), 6.62−6.76 (3H, m, 2′-H, 5′-H and 6′-H), 6.95 (2H, d, J = 8.4 Hz, 3″-H) and 7.15 (2H, d, J = 8.8 Hz, 2″-H); δ_C (100 MHz; $CDCl_3$) −5.3 and −4.6 (2 × CH_3, $SiCH_3$), 10.2 (CH_3, C-2), 11.1 (CH_3, C-3), 18.1 (q, $C(CH_3)_3$), 25.8 (CH_3, $C(CH_3)_3$), 38.3 (CH, C-3), 41.7 (CH, C-2), 55.7 (CH_3, OCH_3), 77.8 (CH, C-1), 78.2 (CH, C-4), 94.4 (CH_2, OCH_2O), 109.6 (CH, C-2′), 110.1 (CH, C-5′), 116.0 (CH, C-3″), 119.1 (CH, C-6′), 127.9 (CH, C-2″), 137.0 and 137.2 (2q, C-1′ and C-1″), 147.8 and 148.4 (2q, C-3′ and C-4′) and 156.5 (q, C-4″); m/z (ESI) 527 (MNa^+, 100%), 355 (24), 235 (14); HRMS (ESI) calcd for $C_{28}H_{44}NaO_6Si$ (MNa^+), 527.2805; found, 527.2792.

(−)-Methoxymethyl pycnanthuligene A, 49. The reaction was carried out according to general procedure E, using alcohol **47** (0.085 g, 0.17 mmol), reaction time was 90 min. A solvent mixture of 9:1 hexanes/ethyl acetate was used for flash chromatography to give the title product (0.034 g, 61%) as a colorless oil. $[\alpha]_D$ = −55 (c 0.2, $CHCl_3$); ν_{max}(neat)/cm^{-1} 2957 (CH), 1606, 1506 (C=C), 1463, 1228, 1148, 1120, 1076, and 1002 (C−O), 921, 865; δ_H (400 MHz; $CDCl_3$) 0.98 (3H, d, J = 8.0 Hz, 9′-CH_3), 1.68 (3H, s, 9-CH_3), 2.25 (1H, m, 8′-H), 3.35 (3H, s, OCH_2OCH_3), 3.59 (1H, d, J = 4.0 Hz, 7′-H), 3.58 and 3.78 (2 × 3H, s, OCH_3), 5.02 (2H, s, OCH_2OCH_3), 6.03 (1H, s, 7-H), 6.46 (1H, s, 3-H), 6.52 (1H, s, 6-H), 6.78 (2H, d, J = 8.0 Hz, 3′-H and 5′-H) and 6.86 (2H, d, J = 8.0 Hz, 2′-H and 6′-H); δ_C (100 MHz; $CDCl_3$) 18.8 (CH_3, C-9′), 22.2 (CH_3, C-9), 42.1 (CH, C-8′), 50.4 (CH, C-7′), 55.9 and 55.9 (3 xCH_3, OCH_3), 94.5 (OCH_2O), 109.0 (CH, C-6), 112.9 (CH, C-3), 116.0 (CH, C-3′ and C-5′), 121.1 (CH, C-7), 127.1 and 127.1 (2q, C-2 and C-8), 128.5 (CH, C-2′ and C-6′), 138.6 and 139.0 (2q, C-1 and C-1′), 147.5 and 147.6 (2q, C-4 and C-5) and 155.5 (q, C-4′); m/z (ESI) 355 (MH^+, 100%) and 338 (10); HRMS (ESI) calcd for $C_{22}H_{27}O_4$, 355.1904; found, 355.1913.

(−)-Pycnanthuligene A, (−)-4. To a stirred solution of 2 M HCl (5 mL) was added ether **49** (32 mg, 0.09 mmol) in methanol (5 mL), and the mixture was stirred for 2 h. The solution was neutralized with 1 M NaOH (10 mL), the aqueous mixture was extracted with diethyl ether (3 × 10 mL), the combined organic fractions were dried ($MgSO_4$), and the solvent was removed *in vacuo*. The crude product was purified by flash chromatography (3:1 hexanes/ethyl acetate) to give the title product (24 mg, 86%) as a colorless oil, which solidified upon standing. $[\alpha]_D$ = −41.0 (c 0.16, EtOH); [lit.[5] $[\alpha]_D$ = +33.8 (c 0.31, EtOH)]; δ_H (400 MHz; $CDCl_3$) 1.07 (3H, d, J = 8.0 Hz, 9′-CH_3), 1.77 (3H, s, 9-CH_3), 2.34 (1H, dq J = 3.0, 7.1 Hz, 8′-H), 3.68 (1H, m, 7′-H), 3.77 (3H, s, 5-OCH_3), 3.87 (3H, s, 4-OCH_3), 4.95 (1H, br s, 4′−OH), 6.12 (1H, s, 7-H), 6.54 (1H, s, 3-H), 6.62 (1H, s, 6-H), 6.67 (2H, d, J = 8.0 Hz, 3′-H) and 6.89 (2H, d, J = 8.0 Hz, 6′-H); δ_C (100 MHz; $CDCl_3$) 18.7 (CH_3, C-9′), 22.2 (CH_3, C-9), 42.2 (CH, C-8′), 50.3 (CH, C-7′), 55.9 (2 × CH_3, OCH_3), 108.9 (CH, C-3), 112.9 and 115.0 (CH, C-2′, C-6′ and C-6), 121.1 (CH, C-7), 127.2 and 127.2 (2q, C-2 and C-8), 128.7 (CH, C-3′ and C-5′), 137.7 and 138.7 (2q, C-1 and C-1′), 147.5 and 147.5 (2q, C-4 and C-5) and 153.8 (q, C-4′); m/z (ESI) 333 (MNa^+, 100%), 311 (MH^+, 55) and 130 (15); HRMS (ESI) calcd for $C_{20}H_{23}O_3$, 311.1642; found, 311.1642. All spectral data were in agreement with the literature values with the exception of assignment of several carbons that should be interchanged.[5]

(1*R*,2*R*,3*S*,4*S*)-1-(3,4-Dimethoxyphenyl)-2,3-dimethyl-4-(4,5-methylenedioxyphenyl)-1-(*tert*-butyldimethylsiloxy) butan-4-o1, 48. The reaction was carried out according to general procedure A, using 1-bromo-3,4-(methylenedioxy)benzene (0.48 g, 2.3 mmol) and *tert*-butyllithium (3.1 mL, 4.6 mmol, 1.5 M in pentane) with aldehyde **41** (0.8 g, 2.1 mmol). A solvent mixture of 4:1 hexanes/ethyl

acetate was used for flash chromatography to give the title product (0.588 g, 59%) as a pale yellow oil. $[\alpha]_D$ = +68 (*c* 1.2, $CHCl_3$); ν_{max}(neat)/cm^{-1} 3519 (OH), 2956, 2857 (CH), 1721, 1594 (C═C), 1486, 1243, 1137, and 1038 (C−O), 935, 835, 734 ;δ_H (400 MHz; $CDCl_3$) −0.33 and −0.00 (2 × 3H, s, $SiCH_3$), 0.56 (3H, d, *J* = 4.0 Hz, 3-CH_3), 0.87 (9H, s, $C(CH_3)_3$), 1.01 (3H, d, *J* = 4.0 Hz, 2-CH_3), 1.51 (1H, m, 3-H), 2.34 (1H, m, 2-H), 3.78 and 3.85 (2 × 3H, s, OCH_3), 4.26 (1H, d, *J* = 8.0 Hz, 4-H), 4.33 (1H, d, *J* = 8.0 Hz, 1-H), 5.93 (2H, m, OCH_2O) and 6.60−6.86 (6H, m, Ar-H); δ_C (100 MHz; $CDCl_3$) −5.2 and −4.6 (2 × CH_3, $SiCH_3$), 10.4 (CH_3, C-2), 11.4 (CH_3, C-3), 18.1 (q, $C(CH_3)_3$), 25.8 (CH_3, $C(CH_3)_3$), 38.4 (CH, C-2), 41.7 (CH, C-3), 55.6 and 55.8 (2 × CH_3, OCH_3), 77.9 (CH, C-4), 78.5 (CH, C-1), 100.9 (CH_2, OCH_2O), 107.1, 107.8, 109.6, and 110.2 (4 × CH, C-2′ and C-5′ and C-3″ and C-6″), 119.0 and 120.3 (2 × CH, C-2″ and C-6′), 137.0 and 137.9 (2q, C-1′ and C-1″), 146.8, 147.7, 147.8, and 148.5 (4q, C-3′, C-4′, C-4″ and C-5″); *m*/*z* (ESI) 527 (MK^+, 25%), 511 (MNa^+, 56), 489 (MH^+, 10), 357 (100) and 399 (75); HRMS (ESI) calcd for $C_{27}H_{41}O_6Si$, 489.2667; found, 489.2671.

(−)-Pycnanthuligene B, (−)-5. The reaction was carried out according to general procedure E, using alcohol **48** (0.27 g, 0.55 mmol). Reaction time was 45 min, and 4:1 hexanes/ethyl acetate was used for flash chromatography to give initially the title product (0.17 g, 90%) as a pale yellow oil. $[\alpha]_D$ = −100.0 (*c* 0.58, EtOH); [lit.[5] $[\alpha]_D$ = +118.5 (*c* 0.34, EtOH)]; ν_{max}(neat)/cm^{-1} 2959 and 2902 (CH), 1605, 1503 (C═C), 1484, 1226, 1148, 1120, and 1035 (C−O), 935, 868, 810; δ_H (400 MHz; $CDCl_3$) 1.07 (3H, d, *J* = 8.0 Hz, 9′-CH_3), 1.78 (3H, s, 9-CH_3), 2.34 (1H, m, 8′-H), 3.65 (1H, d, *J* = 3.0 Hz, 7′-H), 3.79 (3H, s, 4-OCH_3), 3.88 (3H, s, 5-OCH_3), 5.86 (2H, s, OCH_2O), 6.13 (1H, s, 7-H) and 6.50−6.68 (5H, m, Ar-H); δ_C (100 MHz; $CDCl_3$) 18.8 (CH_3, C-9′), 22.2 (CH_3, C-9), 42.2 (CH, C-8′), 50.8 (CH, C-7′), 55.9 (2 × CH_3, OCH_3), 100.7 (CH_2, OCH_2O), 107.9 (CH, C-5′), 108.1 (2 × CH, C-6′ and C-2′), 109.9 (CH, C-3), 112.8 (CH, C-6), 121.1 (CH, C-7), 127.0 and 127.0 (q, C-1 and C-2), 138.6 (q, C-1′), 139.7 (q, C-8), 145.7 (q, C-4′), 147.4 (q, C-3′), 147.6 and 147.7 (q, C-4 and C-5); *m*/*z* (ESI) 361 (MNa^+, 100%), 339 (M^+, 39), 217 (11); HRMS (ESI) calcd for $C_{21}H_{23}O_4$, requires 339.1591; found, 339.1582. All spectral data were in agreement with the literature values.[5] The unstable intermediate 7-*tert*-butyldimethylsilyl-pycnanthuligene B 50 (19 mg, 5%) was also obtained but was converted in quantitative yield to (−)-**5** upon standing in $CDCl_3$ for 5 h. δ_H (400 MHz; $CDCl_3$) 0.04 and 0.14 (2 × 3H, s, Si-CH_3), 0.83 (12H, m, $C(CH_3)_3$ and 9 or 9′-CH_3), 1.01 (3H, d, *J* = 8.0 Hz, 9 or 9′-CH_3), 1.56 (1H, m, 8-H), 2.06 (1H, m, 8′-H), 3.24 (1H, d, *J* = 8.0 Hz, 7′-H), 3.60−3.84 (6H, m, 4-OCH_3 and 5-OCH_3), 4.48 (1H, m, 7-H), 5.86 (2H, s, OCH_2O) and 6.57−6.71 (6H, m, Ar-H); *m*/*z* (ESI) 471 (NaH^+, 5%), 339 (M^+ pycnanthuligene B, 100), 201 (19); HRMS (ESI) calcd for $C_{27}H_{39}O_5Si$, 471.2561; found, 471.2564.

(2*S*,3*R*)-1,1-Bis(3,4-dimethoxyphenyl)-2,3-dimethylpent-4-ene-1-ol, 51. The reaction was carried out according to general procedure A, using **21** (1.93 g, 8.9 mmol) and *tert*-butyllithium (11.8 mL, 18 mmol, 1.5 M) with ketone **22** (2.0 g, 8.0 mmol). A solvent mixture of 4:1 hexanes/ethyl acetate was used for flash chromatography to give the title product (2.1 g, 68%) as a yellow oil. $[\alpha]_D$ = −17.0 (*c* 3.5, $CHCl_3$); ν_{max}(neat)/cm^{-1} 3535 (OH), 2960 and 2936 (CH), 2256, 1591, and 1508 (C═C), 1463, 1252, and 1235 (C−O), 1138 and 1025, 911, 852, 805 and 762; δ_H (400 MHz; $CDCl_3$) 0.96 (3H, d, *J* = 4.0 Hz, 3-CH_3), 1.09 (3H, d, *J* = 8.0 Hz, 2-CH_3), 2.51 (1H, m, 3-H), 2.81 (1H, dd, *J* = 2.0, 8.0 Hz, 2-H), 3.95 (12H, m, 4 × OCH_3), 5.03 (2H, m, 5-CH_2), 5.97 (1H, m, 4-H), 6.89−6.93 (2H, m, 5′-H and 5″-H), 7.10 (1H, t, *J* = 4.0 Hz, 6′-H or 6″-H), 7.12 (1H, t, *J* = 4.0 Hz, 6′-H or 6″-H), 7.17 (1H, d, *J* = 2.0 Hz, 2′-H or 2″-H) and 7.20 (1H, d, *J* = 2.0 Hz, 2′-H or 2″-H); δ_C (100 MHz; $CDCl_3$) 9.1 (CH_3, C-3), 14.5 (CH_3, C-2), 36.9 (CH, C-3), 43.6 (CH, C-2), 55.6 and 55.7 (4 × CH_3, OCH_3), 81.5 (q, C-1), 109.2 and 109.3 (CH, C-2′ and C-2″), 110.5 and 110.6 (CH, C-5′ and C-5″), 112.1 (CH_2, C-5), 117.5 and 117.7 (CH, C-6′ and C-6″), 139.5 and 140.1 (q, C-1′ and C-1″), 144.8 (CH, C-4), 147.2, 147.3, 148.4, and 148.4 (4q, C-3′, C-4′, C-3″ and C-4″); *m*/*z* (ESI) 409 (MNa^+, 100%), 369 (15), 140 (11); HRMS (ESI) calcd for $C_{23}H_{30}NaO_5$, 409.1985; found, 409.1987.

(2*S*,3*R*)-1,1-Bis(3,4-dimethoxyphenyl)-2,3-dimethyl-4-pentene, 52, and (3*R*)-1,1-Bis(3,4-dimethoxyphenyl)-2,3-dimethylpent-1,4-diene, 53. To a solution of alcohol **51** (0.19 g, 0.49 mmol) in DCM (65 mL) under an atmosphere of nitrogen at 0 °C was added triethylsilane (0.63 mL, 3.9 mmol) followed by $BF_3 \cdot OEt_2$ (0.24 mL, 2.0 mmol). The resultant solution was stirred at 0 °C for 30 min. NH_4Cl solution (30 mL) was added, the layers were separated, the aqueous layer was further extracted with DCM (3 × 20 mL) and dried ($MgSO_4$), and the solvent was removed *in vacuo*. The crude product was purified by flash chromatography (2:3 diethyl ether/hexanes) to give **52** (0.18 g, 91%) as a yellow oil. $[\alpha]_D$ = −27 (*c* 3.0, $CHCl_3$); ν_{max}(neat)/cm^{-1} 2961 and 2935 (CH), 2254, 1601, 1509 (C═C), 1441, 1245, 1166, and 1026 (C−O), 908, 646; δ_H (400 MHz; $CDCl_3$) 0.70 (3H, d, *J* = 8.0 Hz, 2-CH_3), 0.87 (3H, d, 8.0 Hz, 3-CH_3), 2.28 (1H, m, 3-H), 2.39 (1H, m, 2-H), 3.56 (1H, d, *J* = 12.0 Hz, 1-H), 3.82, 3.83, and 3.86 (12H, s, OCH_3), 4.95 (2H, m, 5-CH_2), 5.84 (1H, m, 4-H), 6.76−6.86 (6H, m, Ar-H); δ_C (100 MHz; $CDCl_3$) 11.1 (CH_3, C-2), 12.2 (CH_3, C-3), 37.2 (CH, C-3), 40.7 (CH, C-2), 55.7 (4 × CH_3, OCH_3), 111.1 and 111.2 (CH, C-5′ and C-5″ or C-6′ and C-6″), 112.5 and 112.9 (CH, C-2′ and C-2″), 113.4 (CH_2, C-5), 119.5 and 119.7 (CH, C-5′ and C-5″ or C-6′ and C-6″), 135.9 and 136.3 (q, C-1′ and C-1″), 137.2 (q, C-1), 144.3 (CH, C-4), 147.1, 147.3, 148.7, and 148.8 (q, C-3′, C-4′, C-4″ and C-5″); *m*/*z* (ESI) 393 (MNa^+, 35%), 391 (100), 369 (18); HRMS (ESI) calcd for $C_{23}H_{30}NaO_4$, 393.2036; found, 393.2027. Diene **53** (8 mg, 4%) as a yellow oil was obtained in a second fraction. δ_H (400 MHz; CDCl) 1.12 (3H, d, *J* = 8.0 Hz, 3-CH_3), 1.66 (3H, s, 2-CH_3), 3.35 (1H, m, 3-H), 3.81 (12H, s, OCH_3), 5.02 (2H, m, 5-CH_2), 5.91 (1H, m, 4-H), 6.59 (1H, d, *J* = 4.0 Hz, 2′-H or 2″-H), 6.65−6.67 (3H, m, 6′-H, 6″-H and 2′-H or 2″-H) and 6.83 (2H, d, *J* = 8.0 Hz, 5′-H and 5″-H); δ_C (100 MHz; $CDCl_3$) 14.9 (CH_3, C-2), 17.9 (CH_3, C-2), 40.8 (CH, C-3), 55.8 and 55.9 (CH_3, all OCH_3), 111.8 and 112.2 (CH, C-5′ and C-5″ or C-6′ and C-6″), 113.4, 113.7, and 113.9 (CH and CH_2, C-2′, C-2″ and C-5), 122.2 and 122.7 (CH, C-5′ and C-5″ or C-6′ and C-6″), 135.4 and 135.5 (q, C-1′ and C-1″), 136.3 and 137.5 (q, C-1 and C-2), 142.4 (CH, C-4), 143.9, 144.0, 145.9, and 146.0 (q, C-3′, C-3″, C-4′ and C-4″); *m*/*z* (ESI) 391 (NaM^+, 100%), 369 (11); HRMS (ESI) calcd for $C_{23}H_{28}NaO_4$, 391.1885; found, 391.1883.

(2*R*,3*S*)-1,1-Bis(3,4-dimethoxyphenyl)-2,3-dimethyl-4-butanal. Beginning from alkene **52** (0.176 g, 0.48 mmol) dihydroxylation according to general procedure C after flash chromatography using 9:1 DCM/methanol gave the corresponding diol (0.19 g, 94%) as a yellow oil. The diol then underwent a periodate cleavage reaction, according to general procedure D. A solvent mixture of 3:1 ethyl acetate/hexanes was used for flash chromatography to give the title product (0.164 g, 91%) as a pale yellow oil. $[\alpha]_D$ = −51.0 (*c* 3.32, $CHCl_3$); ν_{max}(neat)/cm^{-1} 2933 and 2836 (CH), 1720 (C═O), 1590, 1510 (C═C) 1463, 1262, 1143, 1027 (C−O), 857, 748; δ_H (300 MHz; $CDCl_3$) 0.72 (3H, d, *J* = 8.0 Hz, 2-CH_3), 1.05 (3H, *J* = 8.0 Hz, 3-CH_3), 2.39 (1H, m, 3-H), 3.00 (1H, m, 2-H), 3.56 (1H, d, *J* = 8.0 Hz, 1-H), 3.83, 3.84, 3.86, and 3.88 (12H, s, OCH_3), 6.79−6.89 (6H, m, Ar-H) and 9.65 (1H, s, 4-H); δ_C (100 MHz; $CDCl_3$) 6.5 (CH_3, C-3), 13.7 (CH_3, C-2), 35.6 (CH, C-2), 47.6 (CH, C-3), 55.4, 55.8, and 55.9 (4 × CH_3, OCH_3), 111.0, 111.2, 111.3, and 111.5 (CH, C-2′, C-2″, C-5′ and C-5″), 119.4 and 119.6 (CH, C-6′ and C-6″), 136.2 (q, C-1′ and C-1″), 148.1 and 148.4 (q, C-3′ and C-3″), 205.4 (C═O, C-4); *m*/*z* (ESI) 395 (NaM^+, 100%), 373 (MH^+, 8), 301 (3), 235 (3); HRMS (ESI) calcd for $C_{22}H_{29}O_5$, 373.2010; found, 373.2013.

(−)-Kadangustin J, (−)-8. To a solution of (2*R*,3*S*)-1,1-bis(3,4-dimethoxyphenyl)-2,3-dimethyl-4-butanal (0.16 g, 0.43 mmol) in methanol (5 mL) at −78 °C was added sodium borohydride (0. 64 mg,

1.7 mmol), and the resulting suspension was stirred under an atmosphere of nitrogen at room temperature for 3 h. Water (5 mL) was added, and the methanol was removed *in vacuo*. Further water (5 mL) was added to the residue, and the crude product was extracted with ethyl acetate (3 × 15 mL). The combined organic extracts were dried ($MgSO_4$), the solvent was removed *in vacuo*, and the crude product was purified by flash chromatography (1:1 ethyl acetate/hexanes) to give the title product (0.150 g, 93%) as a colorless oil that solidified upon standing. $[\alpha]_D = -20.7$ (*c* 1.19, MeOH); [lit.[8] $[\alpha]_D = +4.9$ (*c* 0.171, MeOH)]; ν_{max}(neat)/cm^{-1} 3222 (OH), 2959, 2939 (CH), 1591, 1514 (C═C), 1463, 1417, 1262, 1143, 1028 (C−O), 747; δ_H (400 MHz; $CDCl_3$) 0.68 (3H, d, 8.0 Hz, 9-CH_3), 0.74 (3H, d, *J* = 4.0 Hz, 9′-CH_3), 1.75 (1H, m, 8′-H), 2.60 (1H, m, 8-H), 3.45 (2H, m, 7′-CH_2), 3.52 (1H, d, *J* = 12.0 Hz, 7-H), 3.80 (6H, s, OCH_3), 3.84 and 3.85 (6H, s, OCH_3), and 6.74−6.88 (6H, m, Ar-H); δ_C (100 MHz; $CDCl_3$) 9.5 (CH_3, C-9′), 11.7 (CH_3, C-9), 35.8 (CH, C-8), 35.9 (CH, C-8′), 55.7 and 55.7 (4 × CH_3, OCH_3), 77.2 (CH, C-7), 66.8 (CH_2, C-7′), 111.1, 111.2, and 111.3 (CH, C-5, C-5′, C-6 and C-6′), 119.5 and 119.6 (C-2 and C-2′), 137.1 and 137.6 (q, C-1 and C-1′), 147.1 (q, C-4 and C-4′), 148.7 and 148.8 (q, C-3 and C-3′); *m*/*z* (ESI) 397 (MNa^+, 100%), 287 (2), 255 (3), 237 (6); HRMS (ESI) calcd for $C_{22}H_{30}NaO_5$, 397.1985; found, 397.1988. All spectral data were in agreement with the literature values with the exception of assignment of several carbons that should be interchanged.[8]

■ ASSOCIATED CONTENT

Supporting Information. ^{1}H and ^{13}C NMR spectra for compounds (+)-**1**, (−)-**3**, (−)-**4**, (−)-**5**, (−)-**8**, (*R*,*S*)-**9**, **15**, **20**, **22**−**25**, **32**−**36**, **39**−**42**, and **47**−**52**. This material is available free of charge via the Internet at http://pubs.acs.org.

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