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Chiral and Stereoselective Total Synthesis of Novel Immunosuppressant FR65814 from D-Glucose

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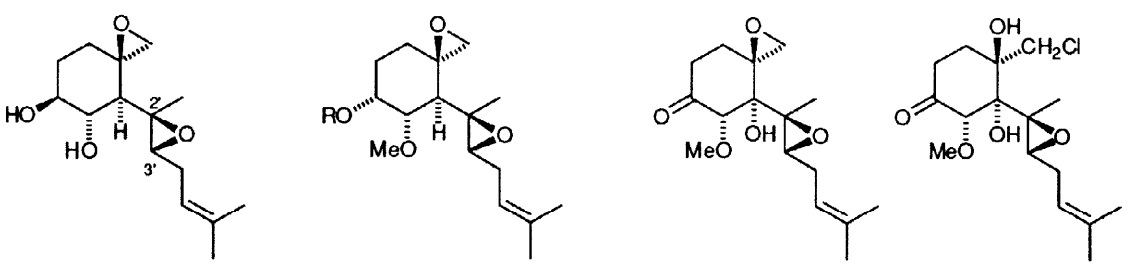
Abstract: The chiral synthesis of the immunosuppressive sesquiterpene, FR65814 **1** is described. The cyclohexane ring in **1** was prepared in an optically active form from D-glucose using Ferrier's carbocyclization reaction, and the carbon side-chain in **1** was stereoselectively introduced via chirality transfer by way of Claisen rearrangement of the cyclohexenol derivative, followed by Pd-catalyzed Stille coupling. The bis-epoxide function was stereoselectively constructed by sulfur ylide chemistry and vanadium catalyzed epoxidation of a homoallyl alcohol derivative. This first total synthesis fully confirmed the proposed absolute structure of FR65814.

Introduction

FR65814 **1** is a sesquiterpene isolated from the culture broth of *Penicillium jensenii* F-2833 and reported to show a potent immunosuppressive activity.[1] The structure of **1** was tentatively assigned[1] on the basis of the spectral similarity to fumagillol **3**, a hydrolysis product of fumagillin **2**, which showed antiparastic and carcinolytic activity.[2] Recent discovery of inhibitory activity of fumagillin against endothelial cell proliferation and tumor-induced angiogenesis attracted the novel biological attention,[3] and compounds related fumagillin, such as TNP-470 **4**, have been expected as the anti-cancer drug candidates.[3] Ovalicin and chlovalicin are also reported to show interleukin 6 dependent cell growth inhibitory activities.[4] Such interesting biological activity as well as their challenging structures which contain a highly functionalized cyclohexane ring with multiple stereocenters, stimulated synthetic efforts and elegant total synthesis of racemic fumagillin by Corey[5a], optically active fumagillol by Kim[5b], and ovalicin (racemic[5c] and optically active[5d]) have been reported to date.



FR65814 (**1**) Fumagillin (**2**): R = C(O)(CH=CH)$_4$CO$_2$H (*E*) Ovalicin (**5**) Chlovalicin (**6**)

Fumagillol (**3**): R = H

TNP-470 (**4**): R = C(O)NHCOCH$_2$Cl

Fig. 1. FR65814 and related sesquiterpenoids.

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However, no report on the synthesis of **1** has appeared. In this article, as a part of our continuous study to synthesize biologically important compounds containing cyclohexane unit starting from aldohexoses utilizing Ferrier's carbocyclization,[6,7] we report the first total synthesis of **1** from D-glucose.[8]

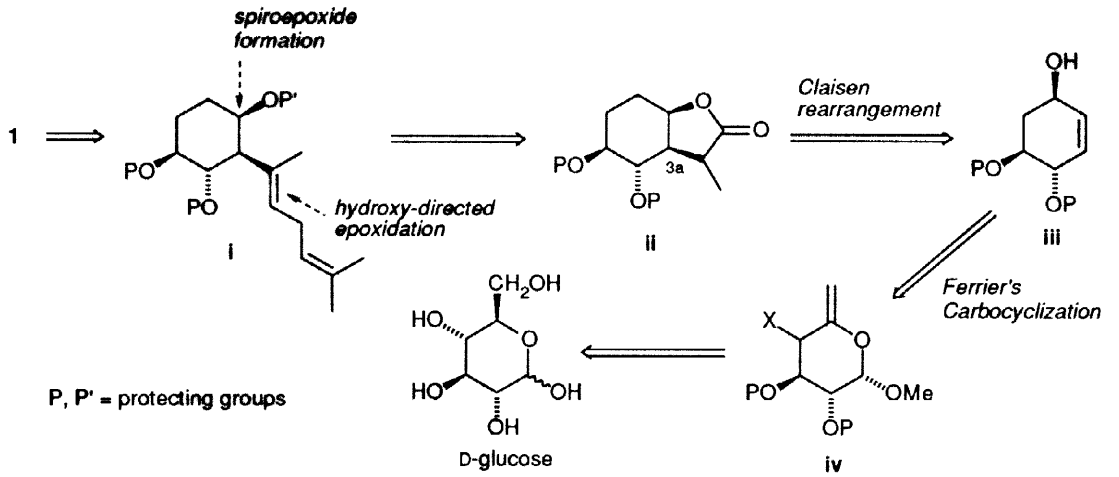


Fig. 2. Retrosynthetic analysis of FR65814.

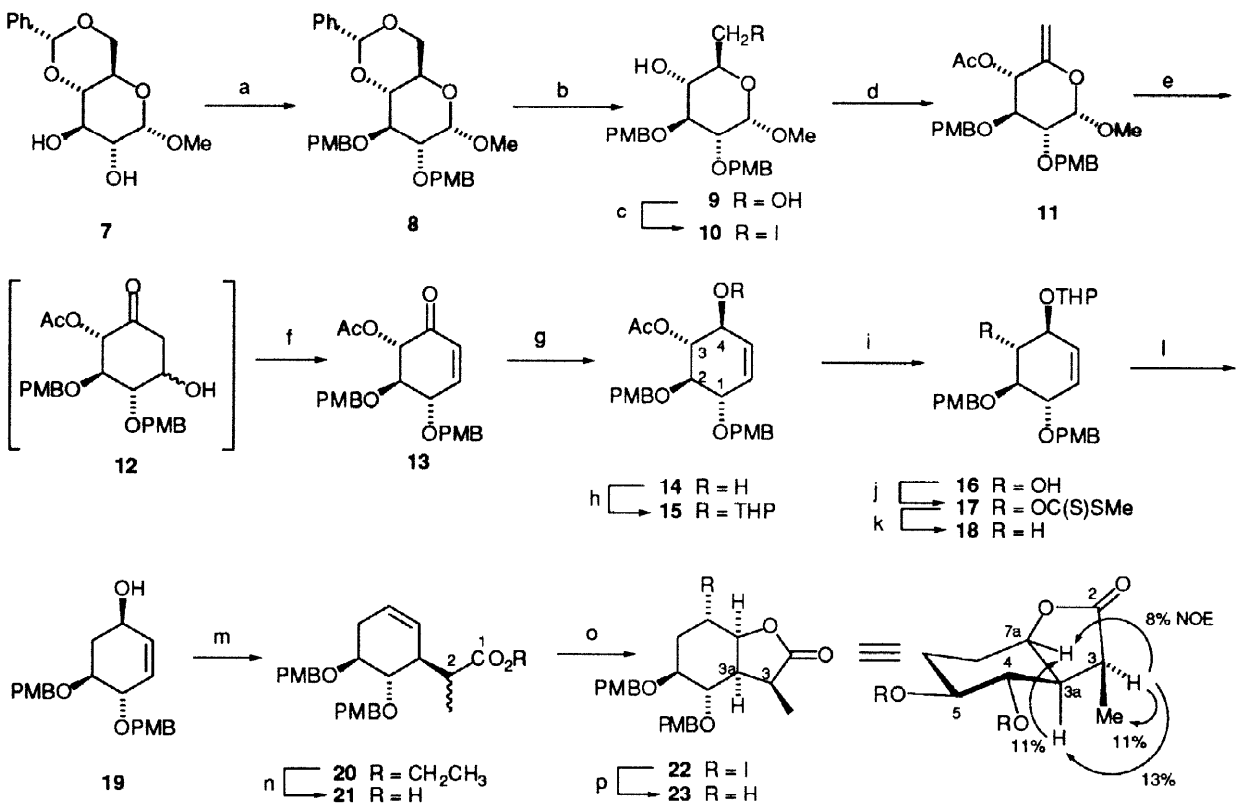
Our retrosynthetic analysis (Fig. 2) suggested that the **1** would be constructed by bis-epoxide formation of homoallylic alcohol with tri-substituted *E*-olefin **i**. Compound **i** was envisioned to be prepared by steroselective carbon-elongation of γ-lactone **ii**, whose C-3a stereochemistry would be generated from cyclohexenol **iii** via chirality transfer by way of [3,3]-sigmatropic rearrangement. The cyclohexenol **iii**, in turn, was expected to arise by catalytic Ferrier's carbocyclization reaction[9] of 6-deoxy-5-enopyranoside derivative **iv**, which should be readily available in an optically pure form from D-glucose.

Results and Discussion

Preparation of the key intermediate, γ-lactone (23): The synthesis of the important intermediate, γ-lactone **23** via cyclohexenol **19**, commenced with commercially available methyl 4,6-*O*-benzylidene-α-D-glucopyranoside **7**. The hydroxy groups in **7** was protected as bis-(4-methoxybenzyl)ether to give **8**, whose 4,6-*O*-benzylidene group was removed by acid hydrolysis to afford **9** (85% from **7**). Treatment of compound **9** with I_2, Ph_3P and imidazole provided primary iodide **10** in 93% yield. Reaction of **10** with *t*-BuOK in tetrahydrofuran (THF) at room temperature, followed by conventional acetylation provided 6-deoxy-5-enopyranoside derivative **11** in 77% yield. Catalytic Ferrier's carbocyclization reaction of **11** using mercury(II) trifluoroacetate (10 mol%)[9a] in acetone–water (2:1) at room temperature cleanly generated the cyclohexanone **12**, which, without purification, was transformed into the enone **13** by the action of methanesulfonyl chloride (MsCl) and triethylamine (84% yield from **11**). Reduction of **13** under the conditions of Luche[10] proceeded stereoselectively and gave cyclohexenol **14** (90% yield). The observed large coupling constants in **14** ($J_{2,3}$ = 10.3 Hz, $J_{3,4}$ = 7.3 Hz) supported the assigned structure possessing pseudo-equatorial hydroxy group. The hydroxy group in **14** was protected as tetrahydropyranyl (THP) ether to afford **15** (90% yield), whose *O*-acetyl group was removed by sodium methoxide in MeOH to give **16** in 87% yield. The hydroxy group in **16** was then deoxygenated via xanthate ester.[11] Treatment of **16** with NaH and CS_2 afforded the xanthate **17**, which, without purification was reacted with *n*-Bu_3SnH to give **18** in 71% yield from **16**. The THP protecting group

was removed by the action of pyridinium *p*-toluenesulfonate (PPTS)[12] in EtOH to generate the desired cyclohexenol **19** in 96% yield.

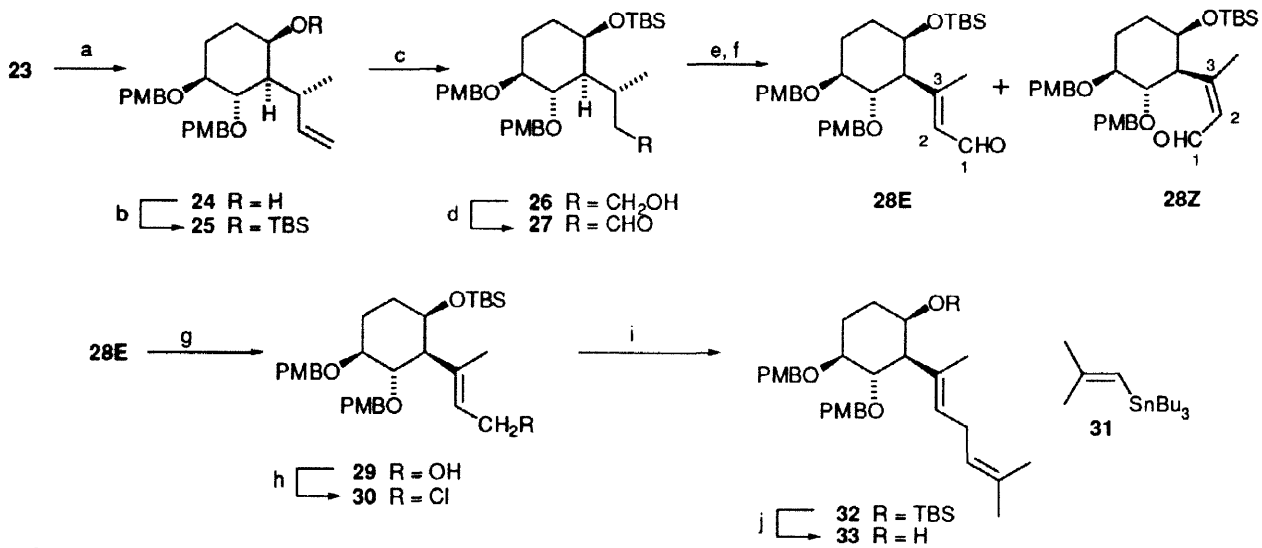
With optically active cyclohexenol **19** in hand, introduction of a carbon side-chain by chirality transfer reaction was next explored. Claisen rearrangement[13] of **19** with triethyl orthopropionate in the presence of a catalytic amount of propionic acid at 140 °C provided rearranged product **20** in 74% yield as an inseparable diastereomeric mixture at C-2 (*ca.* 1:1). Saponification of the ester group in **20** with *t*-BuOK in dimethyl sulfoxide[14] (DMSO) afforded the crude carboxylic acid **21**. Interestingly, epimerization at C-2 occurred during the reaction and carboxylic acid obtained was a sole product, judging from its ^{1}H NMR spectrum. Iodolactonization of the crude carboxylic acid **21** provided γ-lactone **22** in 87% yield from **20** as the single isomer. Deiodination with *n*-Bu_3SnH cleanly afforded **23** in 91% yield. The observed coupling constants ($J_{3a,4}$ = 9.2 Hz, $J_{3a,7a}$ = 4.4 Hz) and NOE between H-3 and H-7a, and H-3a and H-7a in compound **23** clearly revealed that the carbon side-chain at C-3a was introduced in the suprafacial mode, and suggested that the stereochemistry at C-3 should be *S*, as depicted in Scheme 1.



Scheme 1 PMB = 4-methoxybenzyl, THP = tetrahydropyran-2-yl, Reagents and conditions: a, NaH, PMBCl, DMF, 0 °C - r.t.; b, AcOH–H_2O (4:1), 60 °C; c, Ph_3P, I_2, imidazole, toluene, r.t.; d, *t*-BuOK, THF, r.t., then Ac_2O, pyridine, r.t.; e, 10 mol% $Hg(OCOCF_3)_2$, acetone-H_2O (2:1), r.t.; f, MsCl, Et_3N, CH_2Cl_2, 0 °C; g, $NaBH_4$, $CeCl_3 \cdot 7H_2O$, MeOH, 0 °C; h, 3,4-dihydro-2*H*-pyran, PPTS, CH_2Cl_2, r.t.; i, MeONa, MeOH, r.t.; j, NaH, CS_2, imidazole, THF, 0 °C, then MeI; k, *n*-Bu_3SnH, 2,2'-azobisisobutyronitrile (AIBN), toluene, reflux; l, PPTS, EtOH, 50 °C; m, $CH_3CH_2C(OEt)_3$, $CH_3CH_2CO_2H$, 140 °C; n, *t*-BuOK, DMSO, r.t.; o, I_2, KI, THF-aq. $NaHCO_3$, r.t.; p, *n*-Bu_3SnH, AIBN, PhH, reflux.

Elongation of the carbon side-chain: With the γ-lactone **23** which embodies proper hydroxy groups and the carbon-carbon bond with correct stereochemistries on the cyclohexane ring in hand, the elongation of the carbon side-chain was next explored (Scheme 2). Treatment of γ-lactone **23** with

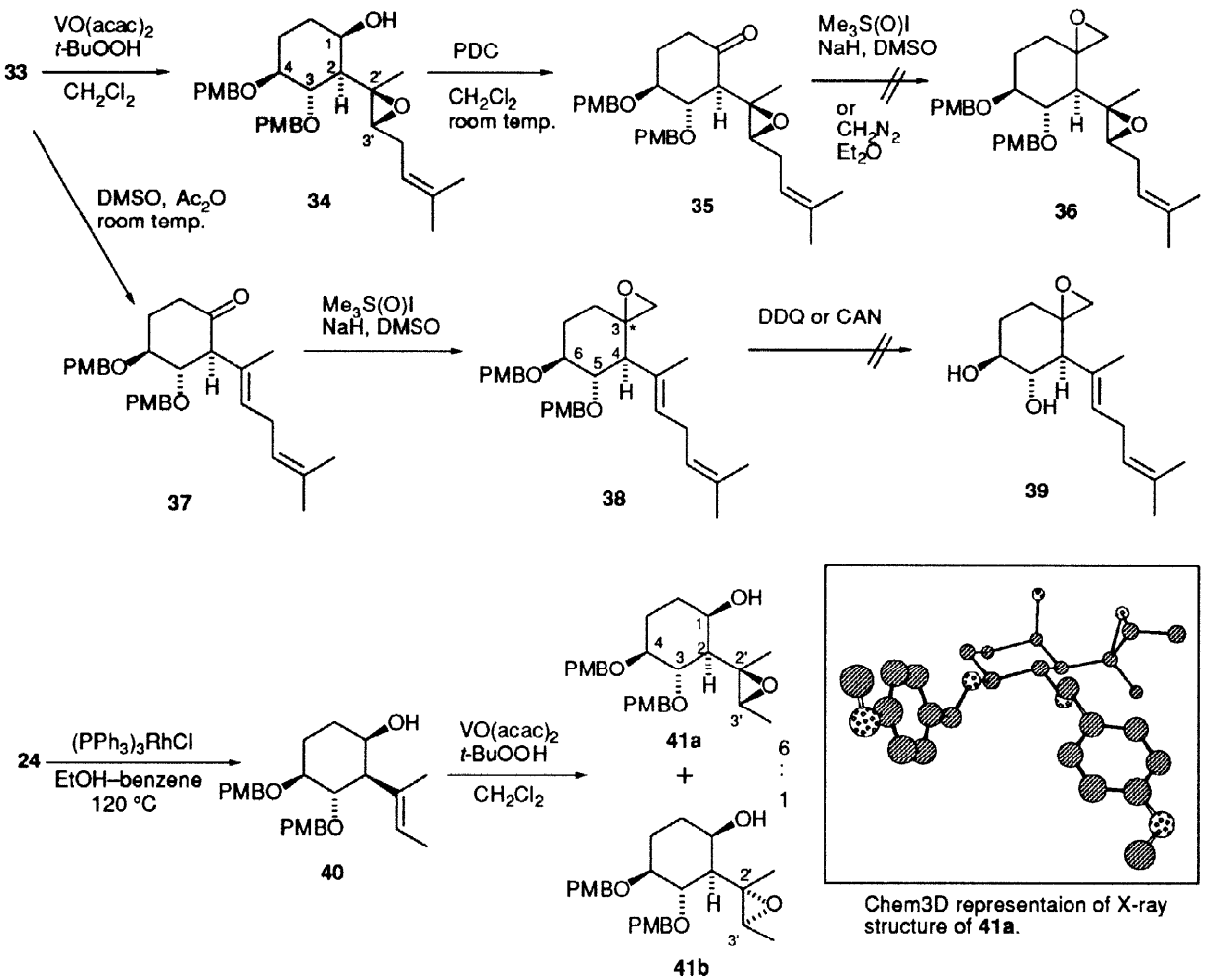
diisobutylaluminium hydride (Dibal) afforded the corresponding lactol, which, without purification, was subjected to Wittig reaction with $Ph_3P{=}CH_2$ to give compound **24** in 90% yield. After protection of the secondary alcohol function as TBDMS ether, the alkene portion of the resulting **25** was converted into primary alcohol by hydroboration-oxidation to provide **26** in 84% yield from **24**. Perruthenate oxidation[15] of **26** gave aldehyde **27** (81%), which was transformed into silyl enol ether by the action of KHMDS and TMSCl. Without purification, the crude silyl enol ether was oxidized with stoichiometric amount of $Pd(OAc)_2$[16] to give α,β-unsaturated aldehyde with *E*-geometry **28E** in 47% yield. The *Z*-isomer **28Z** was also isolated as the minor product (8% yield). The observed NOE between C-3 methyl and a formyl hydrogen in **28E**, and that between C-3 methyl and a vinyl hydrogen in **28Z** clearly assigned the geometries of the double bonds, respectively. Reduction of compound **28E** with Dibal afforded allyl alcohol **29** (93% yield), which was converted into allylic chloride **30** in 93% yield. Stille coupling[17] of **30** with isobutenyltributyltin[18] **31** in the presence of $Pd(PPh_3)_4$ successfully provided the coupling product **32** in 60% yield. Deprotection of the silyl protecting group in **32** afforded homoallyl alcohol **33** in 84% yield.



Scheme 2 TBS = *t*-BuMe$_2$Si-, Reagents and conditions: a, Dibal, toluene, -78 °C, then Ph_3PCH_3Br, *n*-BuLi, THF, 60 °C; TBSOTf, 2,6-lutidine, CH_2Cl_2, 0 °C; c, BH_3·THF, THF, 0 °C, then H_2O_2, aq. NaOH, 0 °C; d, Tetrapropylammonium perruthenate, 4-methylmorpholine *N*-oxide, MS-4A, CH_2Cl_2, r.t.; e, $KN(SiMe_3)_2$, THF, 0 ~ r.t., then $MeSi_3Cl$–Et_3N, r.t; f, $Pd(OAc)_2$, CH_3CN, 0 °C; g, Dibal, toluene, -78 °C; h, MsCl, LiCl, collidine, DMF, r.t.; i, **31**, $Pd(PPh_3)_4$, THF, 40 °C; j, *n*-Bu_4NF, THF, r.t.

Generation of bis-epoxide function; unsuccessful attempts: Having established the preparation of the substituted cyclohexane derivative **33** with the proper carbon side-chain, the stereoselective introduction of the bis-epoxide function was next investigated (Scheme 3). Vanadium-catalyzed epoxidation[19] of **33** generated the single epoxide **34** in 91% yield. The stereochemistry of the newly formed epoxide moiety in **34** was assigned by the comparison of its ^1H NMR spectrum with those of model compounds **41a** and **41b**. These compounds were obtained in a ratio of 6:1 by vanadium-catalyzed epoxidation of **40**, which was prepared from **24** by way of rhodium-catalyzed alkene isomerization.[20] The *E*-geometry of the double bond in **40** was confirmed by observed NOE between methyl groups in the side-chain. In the ^1H NMR spectrum of the major epoxide **41a**, whose structure was unambiguously confirmed by single crystal X-ray analysis (Scheme 3), methine proton at the epoxide moiety (H-3') was observed at δ 3.18 ppm and H-3 was appeared at δ 3.63

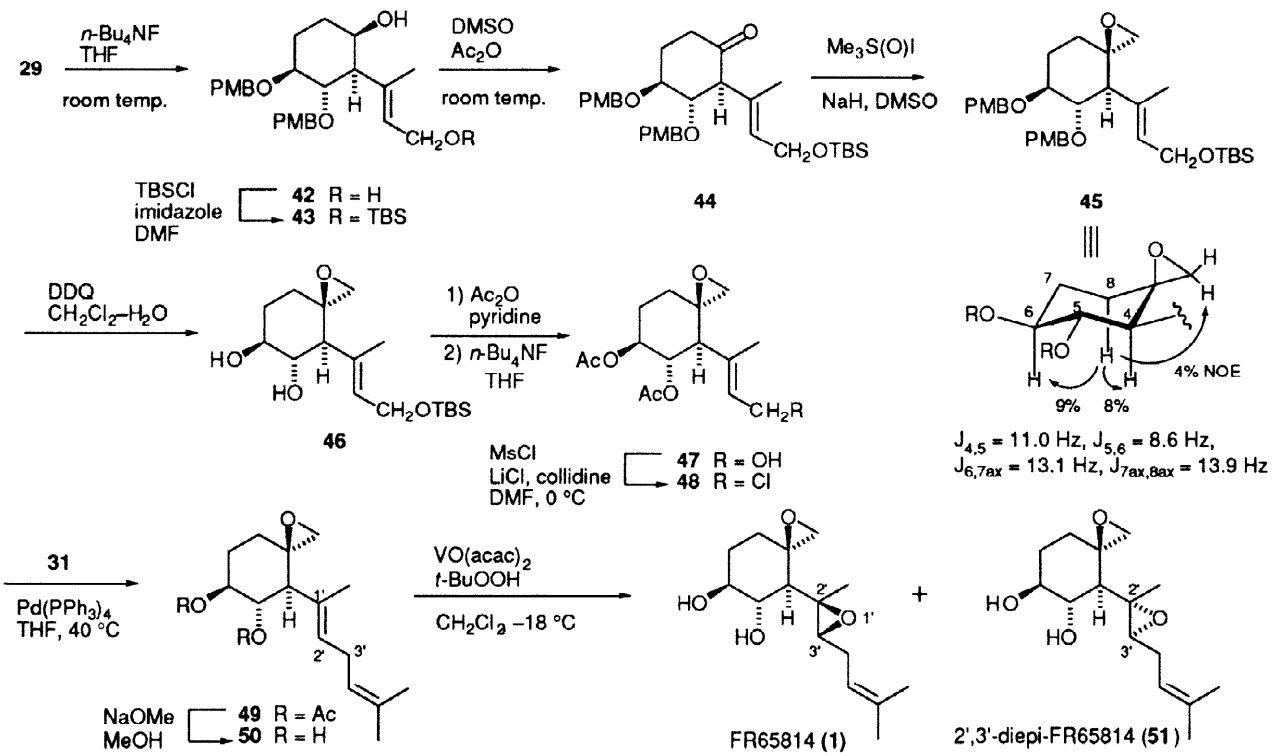
ppm. On the other hand, the resonance of H-3' in the epimer **41b** was observed at δ 2.84 and that of H-3 was observed at δ 3.95 ppm. In the compound **34**, H-3' and H-3 were resonated at δ 3.07 and 3.66 ppm, respectively. The spectral similarity between **34** and **41a** suggested that the stereochemistry of the epoxide moiety in **34** should be 2'*R*, 3'*S*. To complete the total synthesis, formation of the spiro epoxide function was then explored. Oxidation of **34** with pyridinium dichromate (PDC) afforded ketone **35** in 60% yield. Unfortunately, compound **35** was found to be rather unstable, and attempts to convert **35** into spiro epoxide **36** (reaction with dimethyloxosulphonium methylide[21] or CH_2N_2), or to introduce one carbon (reaction with $Ph_3P{=}CH_2$ or Tebbe reagent) resulted in the decomposition of ketone **35**. Alternatively, the hydroxy group in compound **33** was oxidized to give another ketone **37** (63% yield), which was reacted with stabilized sulfur ylide ($Me_2S^+(O)CH_2^-$) to provide **38** as a single isomer (the stereochemistry at C-3 not determined) in 47% yield. Treatment of **38** with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) or ceric ammonium nitrate (CAN) to deprotect *O*-MPM group, however, gave no desired diol **39**.



Scheme 3 acac = $CH_3COCH{=}C(O\text{-})CH_3$.

Total synthesis of FR65814: The failure to construct spiro epoxide function in compound **35** and to deprotect *O*-MPM group in compound **38** led us to examine the another approach. Deprotection of *O*-silyl group in **29** afforded diol **42** quantitatively. Protection of the primary alcohol function gave **43**, whose

secondary alcohol function was oxidized with Ac_2O-DMSO to generate ketone **44** in 83% yield from **42**. Reaction of **44** with stabilized sulfur ylide, which is known to add from the equatorial direction in the cyclohexanone system,[21,22] proceeded stereoselectively and afforded spiro epoxide **45** as the sole product in 58% yield. The observed coupling constants and NOE of **45**, as well as ^1H NMR spectral similarity of a methylene proton at spiro epoxide portion between **45** (δ 2.48, J = 4.9 Hz) and fumagillol (δ 2.47, J = 4.9 Hz) clearly supported the assigned structure (Scheme 4). Treatment of **45** with DDQ afforded diol **46**, whose *O*-acetylation, followed by desilylation provided **47** in 92% yield from **45**. The allyl alcohol **47** was transformed into allylic chloride **48** quantitatively. Stille coupling of **48** with isobutenyltributyltin **31** in the presence of $Pd(PPh_3)_4$ successfully provided the coupling product, *E*-diene **49** in 72% yield. The difference NOE analysis in **49** (NOE between Me at C-1' and C-3' methylene, and H-2' and C-3' methylene; no NOE between Me at C-1' and H-2') showed that the double bond in **49** should be *E* and no isomerization had occurred during the Stille coupling. Removal of the *O*-acetyl group gave diol **50** in 99% yield. The final transformation, introduction of the second epoxide functionality was stereoselectively achieved by vanadium-catalyzed epoxidation[19] to furnish FR65814 **1** in 70% yield. In this reaction, the small amount (9%) of diastereomeric epoxide (**51**: 2',3'-diepi-FR65814) was also isolated. The chemical shifts and appearance of the hydrogen attached to the carbon bearing epoxide ring (H-3') of **1** and **51** in ^1H NMR spectra ($CDCl_3$) are found to be characteristic. Thus, H-3' of FR65814 **1** was observed at δ 2.61 as dd (J = 5.9, 7.1 Hz), whereas that of 2',3'-diepi-FR65814 **51** was appeared δ 3.13 as a broad multiplet. The spectral similarity of the epoxide moiety in **1** to fumagillol (H-3' resonated at δ 2.56 as dd, J = 5.9, 7.1 Hz)[1] strongly suggested that the configuration of C-2' and 3' in **1** should be 2'*R* and 3'*S*.



Scheme 4.

It is noteworthy that the vanadium-catalyzed epoxidation of **33** and **50** both afforded the (2'*R*,3'*S*)-epoxides, **34** and **1**, respectively. Miehlich *et al.*, proposed the chair-like transition state in the vanadium-catalyzed epoxidation of homoallyl alcohol derivatives.[23] Considering Miehlich's hypothesis, the possible rationale for the observed selectivities in the epoxidation of **33** and **50** might be that the presence of non-bonded interactions between an axial oxygen at C-1 and a methyl group at C-1' (TS-a in **33**), and between a methyl at C-1' and a methylene at spiro epoxide (TS-d in **50**), respectively (Fig. 3). Due to these sterically disfavored interactions, TS-b (for **33**) and TS-c (for **50**) would become more favored transition structures, thus affording **34** and **1** in a highly stereoselective manner.

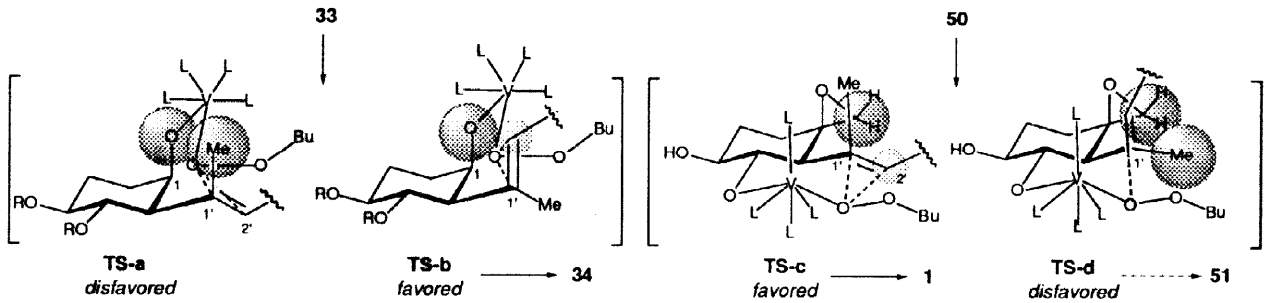


Fig. 3. Transition structure model of vanadium-catalyzed epoxidation of **33** and **50**.

The spectroscopic (^{1}H and ^{13}C NMR) data for synthetic **1** were fully identical with those of natural FR65814,[24] and physical property of synthetic **1** {M.p. 39-40 °C (from Et_2O–hexanes); $[\alpha]_D^{21}$ – 41.6 (*c* 0.25, MeOH)} showed a good accord with those of the natural product {M.p. 39-40 °C (from Et_2O–hexanes)[24]; mixed M.p. 39-40 °C[24]; M.p. 46-47 °C[1]; $[\alpha]_D^{23}$ – 38.4 (*c* 2.4, MeOH)[1]}.

Conclusion

In summary, a chiral and highly stereoselective total synthesis of FR65814 **1** has been achieved. This first total synthesis fully confirmed the assigned structure of FR65814, and revealed that Claisen rearrangement of cyclohexenols derived from carbohydrates by Ferrier's carbocyclization is the potent methodology for the preparation of highly oxygenated terpenes possessing a cyclohexane unit.

Acknowledgments

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EXPERIMENTAL

M.p.s were determined on a Mitamura-riken micro hot stage and are uncorrected. ^{1}H NMR spectra were measured with a JEOL JNM-GSX 270 (270 MHz) or a JEOL JNM-LA 300W (300 MHz) spectrometers, with tetramethylsilane as the internal standard for solutions in deuteriochloroform, unless otherwise noted, and J values are given in Hz. ^{13}C NMR spectra were taken on a JEOL JNM-GSX 270 (67 MHz) or a JEOL JNM-LA 300W (75 MHz) spectrometer. Low and high resolution mass spectra were measured by a JEOL GC Mate spectrometer with EI mode (70 eV). Optical rotations were measured with a JASCO DIP-370 instrument with 1-dm tube and values of $[\alpha]_D$ are recorded in units of 10^{-1} deg cm^2 g^{-1}. IR spectra were taken with a JASCO

FT/IR-200 spectrometer. Organic extracts were dried over anhydrous Na_2SO_4 and concentrated below 40 °C under reduced pressure.

Methyl 4,6-*O*-Benzylidene-2,3-di-*O*-(4-methoxy)benzyl-α-D-glucopyranoside (8). To a suspension of NaH (1.83 g, 76.2 mmol) in DMF (50 ml) at 0 °C was added a solution of methyl 4,6-*O*-benzylidene-α-D-glucopyranoside (7) (8.00 g, 30.5 mmol) in DMF (100 ml). After being stirred for 1 h, to the mixture was added dropwise 4-methoxybenzyl chloride (6.00 ml, 44.3 mmol) at 0 °C, and then stirred at room temperature for 20 h. The reaction mixture was poured into cold saturated aqueous $NaHCO_3$ solution, and further stirred at 0 °C for 1 h . The products was extracted with EtOAc, and the organic layer was concentrated to give a crystalline residue, which was recrystallized from EtOH to afford **8** (15.3 g, 96 %) as a white solid: M.p. 79-82 °C (from EtOH); $[\alpha]_D^{27}$ –40.4 (*c* 1.00, $CHCl_3$); IR γ_{max} (KBr) 1615, 1516 cm^{-1}; ^1H NMR (270 MHz) δ =3.39 (s, 3 H), 3.51 (dd, 1 H, J = 3.7, 9.1 Hz), 3.57 (dd, 1 H, J = 9.1, 9.1 Hz), 3.69 (dd, 1 H, J = 9.9, 10.3 Hz), 3.79, 3.80 (2s, each 3 H), 3.76-3.85 (m, 1 H), 4.00 (dd, 1 H, J = 9.1, 9.1 Hz), 4.25 (dd, 1 H, J = 4.4, 9.9 Hz), 4.52 (d, 1 H, J = 3.7 Hz), 4.62, 4.77, 4.77, 4.82 (4d, each 1 H, J = 11.0 Hz,), 5.54 (s, 1 H), 6.85 (d, 4 H, J = 8.8 Hz), 7.29 (d, 4 H, J = 8.4 Hz), 7.44 (m 5 H); ^{13}C NMR (75 MHz in $CDCl_3$) δ = 55.2, 55.3, 62.3, 69.0, 73.4, 75.0, 78.2, 78.7, 82.1, 99.3, 101.2, 113.7, 113.8, 126.0, 128.2, 128.9, 129.6, 129.7, 130.2, 130.9, 137.4, 159.1, 159.4; MS *m/z* 522 (M^+, 1%), 401 (100), 137 (36), 121(100), 91 (61); HRMS *m/z* 522.2256 (522.2253 calcd for $C_{30}H_{34}O_8$, M^+). Anal. Found: C, 68.97; H, 6.69%. Calcd for $C_{30}H_{34}O_8$: C, 68.95; H, 6.56%.

Methyl 2,3-Di-*O*-(4-methoxy)benzyl-α-D-glucopyranoside (9). A solution of **8** (7.83 g, 15.0 mmol) in acetic acid (120 ml) and water (30 ml) was heated at 60 °C for 2 h. The reaction mixture was concentrated to give a residue. This residue was chromatographed on a column of silica gel (250 g), with acetone-toluene (1:3) as eluent, to afford **9** (5.81 g, 89%) as a colorless syrup: $[\alpha]_D^{29}$ –10.7 (*c* 0.78, $CHCl_3$); IR γ_{max} (neat) 3450, 1610 cm^{-1}; ^1H NMR (270 MHz) δ =1.85 (br, 2 H), 3.37 (s, 3 H), 3.45 (dd, 1 H, J = 3.7, 9.5 Hz), 3.40-3.78 (m, 5 H), 3.80, 3.81 (2s, each 3 H), 4.54 (d, 1 H, J = 3.7 Hz), 4.60, 4.61, 4.72, 4.94 (4d, each 1 H, J = 11.7 Hz), 6.87, 6.88, 7.28, 7.30 (4d, each 2 H, J = 8.6 Hz); ^{13}C NMR (75 MHz in $CDCl_3$) δ = 55.2, 62.4, 70.3, 70.7, 72.8, 74.9, 79.4, 80.9, 98.2, 113.8, 114.0, 129.6, 129.7, 130.1, 130.8, 159.3, 159.4; MS *m/z* 433 (M^+–H, 1%), 313 (30), 137 (33), 121 (100); HRMS *m/z* 433.1862 (433.1862 calcd for $C_{23}H_{29}O_8$, M^+–H). Anal. Found: C, 63.34; H, 7.08%. Calcd for $C_{23}H_{30}O_8$: C, 63.58; H, 6.96%.

Methyl 6-Deoxy-6-iodo-2,3-di-*O*-(4-methoxy)benzyl-α-D-glucopyranoside (10). To a solution of **9** (8.80 g, 20.3 mmol) in toluene (200 ml) were added triphenylphosphine (6.37 g, 24.3 mmol), imidazole (3.31 g, 22.3 mmol) and iodine (5.67 g, 22.3 mmol), and the mixture was stirred at room temperature for 5 h. The reaction mixture was diluted with EtOAc, and successively washed with 20% aqueous $Na_2S_2O_3$ solution, saturated aqueous $NaHCO_3$ solution and brine, and then dried. Removal of the solvent gave a residue, which was chromatographed on a column of silica gel (270 g), with acetone-toluene (1:10) as eluent, to afford **10** (10.2 g, 93%) as a colorless syrup: $[\alpha]_D^{26}$ 24.7 (*c* 0.70, $CHCl_3$); IR γ_{max} (neat) 3480, 1610 cm^{-1}; ^1H NMR (270 MHz) δ=2.37 (s, 1 H), 3.23 (dd, 1 H, J = 7.0, 10.6 Hz), 3.27 (dd, 1 H, J = 2.2, 8.8 Hz), 3.37 (ddd, 1 H, J = 2.2, 2.6, 7.0 Hz), 3.43 (s, 3 H), 3.48 (dd, 1 H, J = 3.7, 9.5 Hz), 3.51 (dd, 1 H, J = 2.6, 10.6 Hz), 3.73 (dd, 1 H, J = 8.8, 9.5 Hz), 3.81 (s, 6 H), 4.57 (d, 1 H, J = 3.7 Hz), 4.59 (d, 1 H, J = 11.0 Hz), 4.60 and 4.72 (2d, each 1 H, J = 11.7 Hz), 4.94 (d, 1 H, J = 11.0 Hz), 6.89 (m, 4 H), 7.28 (m, 4 H); ^{13}C NMR (75 MHz in $CDCl_3$) δ = 55.2, 55.5, 69.8, 72.8, 73.6, 74.9, 79.4, 80.2, 98.2, 113.9, 114.1, 129.7, 129.9, 130.6, 159.4, 159.5; MS *m/z* 423 (M^+–PMB, 97%), 137 (95), 121 (100); HRMS *m/z* 423.0304 (423.0305 calcd for $C_{15}H_{20}O_6I$, M^+–PMB). Anal. Found: C, 50.50; H, 5.62%. Calcd for $C_{23}H_{29}O_7I$: C, 50.75; H, 5.37%.

Methyl 4-*O*-Acetyl-6-deoxy-2,3-di-*O*-(4-methoxy)benzyl-α-D-*xylo*-hex-5-enopyranoside (11). To a solution of **10** (104 mg, 0.191 mmol) in THF (2 ml) was added potassium *tert*-butoxide (64.3 mg, 0.573 mmol), and the mixture was stirred at room temperature for 23 h. The mixture was concentrated to give a residue, which was treated with acetic anhydride (0.7 ml) and pyridine (1.4 ml). After being stirred at room temperature for 3 h, the reaction mixture was concentrated to give a residue, which was diluted with EtOAc, and successively washed with 1 mol dm^{-3} aqueous HCl solution, saturated aqueous $NaHCO_3$ solution, and brine, and then dried. The organic layer was concentrated to give a residue, which was chromatographed on a column of silica gel (3.5 g), with acetone-hexanes (1:5, containing 1 vol% Et_3N) as eluent, to afford **11** (67.7 mg, 77%) as a colorless syrup: $[\alpha]_D^{28}$ –19.1 (*c* 1.14, $CHCl_3$); IR γ_{max} (neat) 1740, 1660, 1610 cm^{-1}; ^1H NMR

(270 MHz) δ = 2.05 (s, 3 H), 3.41 (s, 3 H), 3.64 (dd, 1 H, J = 3.7, 9.5 Hz), 3.80, 3.81 (2s, each 3 H), 3.92 (dd, 1 H, J = 9.5, 9.5 Hz), 4.44 (dd, 1 H, J = 1.8, 1.8 Hz), 4.57-4.65 (m, 4 H), 4.76, 4.79 (2d, each 1 H, J = 11.7 Hz), 6.87 (d, 4 H, J = 8.8 Hz), 7.22, 7.28 (2d, each 2 H, J = 8.8 Hz). Anal. Found: C, 65.24; H, 6.82%. Calcd for $C_{25}H_{30}O_8$: C, 65.49; H, 6.60%.

(4*S*,5*R*,6*S*)-6-Acetoxy-4,5-di-(4-methoxybenzyl)oxy-cyclohex-2-en-1-one (13). To a solution of compound **11** (1.38 g, 3.01 mmol) in acetone (20 ml) and water (10 ml) was added mercury(II) trifluoroacetate (128 mg, 0.301 mmol), and the mixture was stirred at room temperature for 15 h. The reaction mixture was partially concentrated and the products were extracted with EtOAc. The organic layer was washed with 10% aqueous KI solution and 20% aqueous $Na_2S_2O_3$ solution, and then dried. Removal of the solvent gave crude **12** (1.34 g, 100%). This was used for next reaction without further purification. To a solution of crude **12** (1.34 g) in CH_2Cl_2 (15 ml) at 0 °C were added methanesulfonyl chloride (0.699 ml, 9.03 mmol) and triethylamine (2.52 ml, 18.1 mmol), and the mixture was stirred at 0 °C for 2 h. The reaction mixture was diluted with CH_2Cl_2 and successively washed with 0.5 mol dm^{-3} aqueous H_2SO_4 solution, saturated aqueous $NaHCO_3$ solution, and brine, and then dried. Removal of the solvent gave a residue, which was chromatographed on a column of silica gel (50 g), with EtOAc-toluene (1:10) as eluent, to afford **13** (1.07 g, 84%) as a colorless syrup: $[\alpha]_D^{22}$ 83.4 (*c* 0.99, $CHCl_3$); IR γ_{max} (neat) 1750, 1695, 1615, 1515 cm^{-1}; ^1H NMR (270 MHz) δ = 2.16, 3.80, and 3.81 (3s, each 3 H), 3.99 (dd, 1 H, J = 8.4, 11.0 Hz), 4.41 (ddd, 1 H, J = 2.2, 2.2, 8.4 Hz), 4.68, 4.71, 4.76, 4.78 (4d, each 1 H, J = 11.0 Hz), 5.39 (d, 1 H, J = 11.0 Hz), 6.05 (dd, 1 H, J = 2.2, 10.6 Hz), 6.83 (dd, 1 H, J = 2.2, 10.6 Hz), 6.87, 6.89, 7.24, 7.28 (4d, each 2 H, J = 8.8 Hz); ^{13}C NMR (75 MHz in $CDCl_3$) δ = 20.6, 55.2, 73.3, 74.9, 78.6, 82.2, 113.8, 113.9, 127.4, 129.3, 129.5, 129.6, 129.9, 148.8, 159.3, 159.5, 169.8, 192.1; MS *m/z* 426 (M^+, 5%), 305 (100), 137 (100), 121 (100); HRMS *m/z* 426.1679 (426.1678 calcd for $C_{24}H_{26}O_7$, M^+). Anal. Found: C, 67.88; H, 6.19%. Calcd for $C_{24}H_{26}O_7$: C, 67.59; H, 6.15%.

(1*S*,4*S*,5*R*,6*R*)-2-Acetoxy-4,5-di-(4-methoxybenzyl)oxy-cyclohex-2-en-1-ol (14). To a solution of compound **13** (63.7 mg, 0.149 mmol) and $CeCl_3 \cdot 7H_2O$ (83.5 mg, 0.224 mmol) in methanol (2 ml) at 0 °C was added $NaBH_4$ (6.2 mg, 0.164 mmol). After being stirred at 0 °C for 15 min, the mixture was diluted with water and the products were extracted twice with EtOAc. The combined organic layer was washed with brine, and then dried. Removal of the solvent gave a residue, which was chromatographed on a column of silica gel (3 g), with EtOAc-hexanes (1:1) as eluent, to afford **14** (57.6 mg, 90%) as a colorless syrup: $[\alpha]_D^{23}$ 59.8 (*c* 0.85, $CHCl_3$); IR γ_{max} (neat) 3450, 1735, 1610 cm^{-1}; ^1H NMR (270 MHz) δ = 2.07 (s, 3 H), 2.70 (br, 1 H), 3.71 (dd, 1 H, J = 7.3, 10.3 Hz), 3.79 (s, 6 H), 4.18 (m, 1 H), 4.28 (m, 1 H), 4.59 (s, 2 H), 4.66 and 4.75 (2d, each 1 H, J = 11.2 Hz), 4.96 (dd, 1 H, J = 7.3 10.3 Hz), 5.70 (m, 2 H), 6.86 (d, 4 H, J = 8.4 Hz), 7.22 and 7.24 (2d, each 2 H, J = 8.4 Hz); ^{13}C NMR (75 MHz in $CDCl_3$) δ = 21.1, 55.2, 71.0, 72.1, 74.6, 78.9, 79.9, 113.7, 113.8, 127.3, 129.1, 129.3, 129.5, 130.1, 130.4, 159.2, 159.3, 171.7; MS *m/z* 428 (M^+, 0.2%), 307 (99), 171 (100), 137 (100), 121 (100); HRMS *m/z* 428.1837 (428.1835 calcd for $C_{24}H_{28}O_7$, M^+). Anal. Found: C, 67.03; H, 6.70%. Calcd for $C_{24}H_{28}O_7$: C, 67.27; H, 6.59%.

(3*S*,4*R*,5*R*,6*S*)-5-Acetoxy-3,4-di-(4-methoxybenzyl)oxy-6-(tetrahydropyran-2-yl)oxy-cyclohex-1-ene (15). To a solution of compound **14** (1.59 g, 3.71 mmol) and pyridinium *p*-toluenesulfonate (9.3 mg, 0.037 mmol) in CH_2Cl_2 (32 ml) was added 3,4-dihydro-2*H*-pyran (1.02 ml, 11.1 mmol), and the mixture was stirred at room temperature for 24 h. The reaction mixture was diluted with CH_2Cl_2 and washed with brine, and then dried. Removal of the solvent gave a residue, which was chromatographed on a column of silica gel (60 g), with EtOAc-hexanes (1:3) as eluent, to afford **15** (1.88 g, 90%) as a colorless syrup. This compound **15** was obtained diastereomeric mixture (*ca.* 3:1): IR γ_{max} (neat) 1750, 1610 cm^{-1}; ^1H NMR (270 MHz) δ = 1.40-1.80 (m, 6 H), 2.03 (s, 3 H), 3.50 (m 1 H), 3.67 (dd, 1 H, J = 7.9, 10.8 Hz), 3.80 (s, 6 H), 3.80 (m, 1 H), 4.24 (m, 1 H), 4.38 (m, 1 H), 4.60-4.81 (m, 5 H), 5.21 (dd, 1 H, J = 8.1, 10.8 Hz), 5.70 (m, 2 H), 6.86 and 7.24 (2d, each 4 H, J = 8.4 Hz); MS *m/z* 427 (M^+–THP, 13%), 391 (13), 307 (18), 255 (34), 171 (19), 137 (44), 121 (100), 85 (100); HRMS *m/z* 427.1753 (427.1756 calcd for $C_{24}H_{27}O_7$, M^+–THP). Anal. Found: C, 67.79; H, 7.21%. Calcd for $C_{29}H_{36}O_8$: C, 67.95; H, 7.28%.

(1*R*,2*S*,5*S*,6*S*)-5,6-Di-(4-methoxybenzyl)oxy-2-(tetrahydropyran-2-yl)oxy-cyclohex-3-en-1-ol (16). To a solution of compound **15** (1.11 g, 2.17 mmol) in MeOH (22 ml) was added NaOMe (351 mg, 6.50 mmol), and the mixture was stirred at room temperature for 15 h. The reaction mixture was neutralized

with IR-120 resin (H^+) and the insoluble material was removed by filtration. The filtrate was concentrated to give a residue, which was chromatographed on a column of silica gel (40 g), with EtOAc-hexanes (1:4, containing 1 vol% Et_3N) as eluent, to afford **16** (883 mg, 87%; *ca* 3:1 diastereomeric mixture) as a colorless syrup: IR γ_{max} (neat) 3400, 1610 cm^{-1}; ^1H NMR (270 MHz) δ = 1.50-1.90 (m, 6 H), 3.67 (dd, 1 H, J = 7.9, 10.8 Hz), 3.50-4.95 (m, 11 H), 3.79 and 3.80 (2s, each 3 H), 5.56-5.73 (m, 2 H), 6.86, 6.88, 7.31, 7.33 (4d, each 2 H, J = 8.8 Hz); MS *m/z* 385 (M^+–THP, 3%), 349 (27), 265 (22), 213 (22), 171 (19), 137 (100), 121 (100), 85 (100); HRMS *m/z* 385.1651 (385.1651 calcd for $C_{22}H_{25}O_6$, M^+–THP). Anal. Found: C, 68.97; H, 7.44%. Calcd for $C_{27}H_{34}O_7$: C, 68.92; H, 7.28%.

(3*S*,4*S*,6*R*)-3,4-Di-(4-methoxybenzyl)oxy-6-(tetrahydropyran-2-yl)oxy-cyclohex-1-ene (18). To a solution of compound **16** (2.55 g, 5.42 mmol) in THF (50 ml) at 0 °C were added imidazole (36.9 mg, 0.542 mmol) and NaH (60% in oil, 434 mg, 10.8 mmol), and the resulting mixture was stirred at 0 °C for 40 min. To the mixture was added CS_2 (2.44 ml, 40.6 mmol) at 0 °C, and the mixture was further stirred at 0 °C for 1.5 h. To the mixture was then added MeI (675 ml, 10.8 mmol), and the mixture was stirred at 0 °C for 30 min. The reaction was quenched with ice-water, and the products were extracted with EtOAc. The organic layer was dried and concentrated to give a crude xanthate derivative **17** (3.04 g), which was used for next reaction without further purification. A solution of crude **17** (3.04 g), azobisisobutyronitrile (445 mg, 2.71 mmol), and *n*-Bu_3SnH (1.60 ml, 5.96 mmol) in toluene (50 ml) was heated under reflux for 15 h. After cooling, the reaction mixture was concentrated to give a residue, which was chromatographed on a column of silica gel (100 g), with EtOAc-toluene (1:10) as eluent, to afford compound **18** (1.75 g, 71%; ca 3:1 diastereomeric mixture) as a colorless syrup: IR γ_{max} (neat) 1610 cm^{-1}; ^1H NMR (270 MHz) δ = 1.50-1.90 (m, 7 H), 2.48 (m, 1 H), 3.53 (m, 1 H), 3.60 (ddd, 1 H, J = 3.7, 4.8, 7.7 Hz), 3.80 (s, 6 H), 3.89, 4.13, 4.37, and 4.61 (4m, each 1 H), 4.62 (s, 2 H), 4.68 (d, 1 H, J = 11.0 Hz), 4.77 (s, 1 H), 5.71 (m, 1 H), 5.80 (ddd, 1 H, J = 1.8, 1.8, 10.3 Hz), 6.86 (d, 4 H, J = 8.4 Hz), 7.27 (d, 4 H, J = 8.8 Hz); MS *m/z* 369 (M^+–THP, 17%), 333 (6), 249 (42), 197 (11), 137 (100), 121 (89), 85 (100); HRMS *m/z* 369.1703 (369.1702 calcd for $C_{22}H_{25}O_5$, M^+–THP). Anal. Found: C, 71.30; H, 7.41%. Calcd for $C_{27}H_{34}O_6$: C, 71.34; H, 7.54%.

(1*R*,4*S*,5*S*)-4,5-Di-(4-methoxybenzyl)oxy-cyclohex-2-en-1-ol (19). A solution of **18** (519 mg, 1.14 mmol) and pyridinium *p*-toluenesulfonate (28.7 mg, 0.114 mmol) in EtOH (10 ml) was stirred at 50 °C for 3 h. After cooling, the reaction mixture was concentrated to give a residue, which was chromatographed on a column of silica gel (18 g), with EtOAc-toluene (1:4) as eluent, to afford compound **19** (404 mg, 96%) as a colorless syrup: $[\alpha]_D^{22}$ 123 (*c* 1.20, $CHCl_3$); IR γ_{max} (neat) 3400, 1610 cm^{-1}; ^1H NMR (270 MHz) δ = 1.89 (ddd, 1 H, J = 5.5, 7.8, 13.6 Hz), 2.22 (ddd, 1 H, 2.6, 5.1, 13.6 Hz), 2.45 (m, 1 H), 3.78 (ddd, 1 H, J = 2.6, 4.8, 7.8 Hz), 3.81 (s, 6 H), 3.90 and 4.17 (2m, each 1 H), 4.55 (s, 4 H), 5.78 (ddd, 1 H, J = 0.7, 3.7, 10.3 Hz), 5.97 (ddd, 1 H, J = 1.1, 3.7, 10.3 Hz), 6.87 and 7.24 (2d, each 4 H, J = 8.8 Hz); ^{13}C NMR (75 MHz in $CDCl_3$) δ = 34.2, 55.6, 65.4, 71.7, 75.0, 76.6, 77.6, 114.1, 114.2, 127.1, 129.6, 129.7, 130.6, 130.8, 133.3, 159.6; MS *m/z* 370 (M^+, 2%), 249 (100), 137 (100), 121 (100); HRMS *m/z* 370.1781 (370.1780 calcd for $C_{22}H_{26}O_5$, M^+). Anal. Found: C, 71.06; H, 7.26%. Calcd for $C_{22}H_{26}O_5$: C, 71.33; H, 7.07%.

Ethyl 2-{(1*S*,5*S*,6*S*)-5,6-Di-(4-methoxybenzyl)oxy-cyclohex-2-en-1-yl}propionate (20). A solution of **19** (247 mg, 0.668 mmol) and propionic acid (10 µl) in triethyl orthopropionate (10 ml) was stirred at 140 °C for 2 h. After cooling, the reaction mixture was concentrated to give a residue, which was chromatographed on a column of silica gel (8 g), with EtOAc-toluene (1:20) as eluent, to afford compound **20** (223 mg, 74%) as a colorless syrup. This compound was a diastereomeric mixture at C-2 (*ca.* 1:1): IR γ_{max} (neat) 1720, 1610 cm^{-1}; ^1H NMR (270 MHz) δ = 0.88 (d, 1.5 H, J = 7.0 Hz), 1.17 (d, 1.5 H, J = 7.0 Hz), 1.18 (t, 1.5 H, J = 7.1 Hz), 1.22 (t, 1.5 H, J = 7.1 Hz), 2.12 (m, 1 H), 2.48 (m, 0.5 H), 2.54 (m, 1 H), 2.81-2.92 (m, 1.5 H), 3.42 (dd, 0.5 H, J = 9.0, 9.0 Hz), 3.64-3.76 (m, 1 H), 3.80 (s, 6 H), 4.01 (dd, 0.5 H, J = 7.3, 7.3 Hz), 4.10, 4.11 (2q, each 1 H, J = 7.1 Hz), 4.44 and 4.59 (2d, each 0.5 H, J = 10.3 Hz), 4.62 and 4.63 (2s, each 1 H), 4.93 and 4.98 (2d, each 0.5 H, J = 10.3 Hz), 5.32-5.47 (m, 1 H), 5.58 (m, 1 H), 6.86, 6.87, 7.28, 7.30 (4d, each 2 H, J = 8.8 Hz); ^{13}C NMR (75 MHz in $CDCl_3$) δ = 10.8, 14.2, 32.0, 38.3, 19.1, 44.9, 47.3, 55.3, 60.1, 60.3, 71.7, 74.0, 74.4, 78.7, 79.5, 79.8, 80.0, 113.6, 113.7, 113.8, 124.8, 125.5, 125.9, 126.3, 129.2, 129.7, 129.8, 130.9, 131.3, 159.1, 159.2, 174.7, 175.9; MS *m/z* 454 (M^+, 1%), 453 (2), 333 (11), 197 (37), 137 (31), 121 (100); HRMS *m/z* 454.2350 (454.2355 calcd for $C_{27}H_{34}O_6$, M^+). Anal. Found: C, 71.12; H, 7.63%. Calcd for $C_{27}H_{34}O_6$: C, 71.34; H, 7.54%.

(3*S*,3a*S*,4*S*,5*S*,7*S*,7a*S*)-7-Iodo-4,5-di-(4-methoxybenzyl)oxy-3-methyl-3a,4,5,6,7,7a-hexahydrobenzo[*b*]furan-2(3*H*)-one (22). To a solution of **20** (219 mg, 0.482 mmol) in DMSO (5 ml) was added potassium *tert*-butoxide (270 mg, 2.41 mmol), and the mixture was stirred at room temperature for 25 min. The reaction mixture was poured into ice-water. The solution was acidified (pH ~ 2) by addition of 1 mol dm^{-3} aqueous HCl solution, and the products were extracted with EtOAc. The organic layer was dried and then concentrated to give a crude carboxylic acid derivative **21** [205 mg; ^{1}H NMR (270 MHz) δ = 0.88 (d, 3 H, J = 7.1 Hz), 2.10 (m, 1 H), 2.52 (ddd, 1 H, J = 4.9, 5.4, 17.3 Hz), 2.84 (m, 2 H), 3.42 (dd, 1 H, J = 9.0, 9.0 Hz), 3.74 (m, 1 H), 3.79 and 3.80 (2s, each 3 H), 4.59 (d, 1 H, J = 11.1 Hz), 4.63 (s, 2 H), 4.94 (d, 1 H, J = 11.1 Hz), 5.34 (m, 1 H), 5.59 (m, 1 H), 6.86, 6.87, 7.27, and 7.29 (4d, each 2 H, J = 8.8 Hz)], which was used for next reaction without further purification. To a solution of crude **21** (205 mg) in THF (3 ml) and 0.5 mol dm^{-3} aqueous $NaHCO_3$ solution (9 ml) were added KI (798 mg, 4.81 mmol) and iodine (366 mg, 1.44 mmol), and the mixture was stirred at room temperature for 2 h. The reaction mixture was quenched with 20% aqueous $Na_2S_2O_3$ solution, and the products were extracted with EtOAc and CH_2Cl_2. The combined organic layer was dried and concentrated to give a residue, which was chromatographed on a column of silica gel (10 g), with EtOAc-toluene (1:20) as eluent, to afford compound **22** (230 mg, 87%) as a colorless syrup: $[\alpha]_D^{22}$ 14.2 (*c* 1.11, $CHCl_3$); IR γ_{max} (neat) 1780, 1615, 1515 cm^{-1}; ^{1}H NMR (270 MHz) δ = 1.34 (d, 3 H, J = 6.6 Hz), 1.82 (ddd, 1 H, J = 3.5, 11.2, 14.8 Hz), 2.23 (m, 1 H), 2.88 (m, 2 H), 3.48 (dd, 1 H, J = 9.0, 9.0 Hz), 3.80 (s, 6 H), 4.11 (ddd, 1 H, J = 3.5, 9.0, 11.2 Hz), 4.42 (d, 1 H, J = 10.6 Hz), 4.53 and 4.60 (2d, each 1 H, J = 11.0 Hz), 4.65 (m, 2 H), 5.07 (d, 1 H, J = 10.6 Hz), 6.86, 6.87, 7.18, and 7.27 (4d, each 2 H, J = 8.6 Hz); ^{13}C NMR (75 MHz in $CDCl_3$) δ = 10.9, 22.0, 32.4, 42.4, 43.8, 55.3, 71.2, 73.4, 78.1, 80.2, 82.2, 113.8, 113.9, 129.3, 129.7, 129.9, 130.5, 159.1, 159.3, 178.0; MS *m/z* 552 (M^+, 0.1%), 431 (100); HRMS *m/z* 552.1003 (552.1009 calcd for $C_{25}H_{29}O_6I$, M^+). Anal. Found: C, 54.59; H, 5.31%. Calcd for $C_{25}H_{29}O_6I$: C, 54.36; H, 5.29%.

(3*S*,3a*S*,4*S*,5*S*,7a*R*)-4,5-Di-(4-methoxybenzyl)oxy-3-methyl-3a,4,5,6,7,7a-hexahydrobenzo[*b*]furan-2(3*H*)-one (23). A solution of **22** (462 mg, 0.836 mmol), azobisisobutyronitrile (68.7 mg, 0.418 mmol), and *n*-Bu_3SnH (247 ml, 0.920 mmol) in benzene (10 ml) was heated under reflux for 2 h. After cooling, the reaction mixture was diluted with CH_2Cl_2 and washed with saturated aqueous KF solution, and then dried. Removal of the solvent gave a residue, which was chromatographed on a column of silica gel (15 g), with EtOAc-toluene (1:15) as eluent, to afford compound **23** (324 mg, 91%) as a colorless solid: M.p. 95-96 °C (from EtOH); $[\alpha]_D^{28}$ 43.9 (*c* 1.03, $CHCl_3$); IR γ_{max} (KBr) 1760, 1610 cm^{-1}; ^{1}H NMR (270 MHz) δ = 1.34 (d, 3 H, J = 7.3 Hz), 1.49-1.65 (m, 2 H), 1.96 and 2.25 (2m, each 1 H), 2.43 (ddd, 1 H, J = 4.4, 6.6, 9.2 Hz), 2.89 (dq, 1 H, J = 6.6, 7.3 Hz), 3.48 (dd, 1 H, J = 6.6, 9.2 Hz), 3.48 (m, 1 H), 3.80 (s, 6 H), 4.42 (d, 1 H, J = 10.6 Hz), 4.44 (m, 1 H), 4.50 and 4.64 (2d, each 1 H, J = 11.0 Hz), 5.10 (d, 1 H, J = 10.6 Hz), 6.85, 6.86, 7.17, and 7.26 (4d, each 2 H, J = 8.8 Hz); ^{13}C NMR (75 MHz in $CDCl_3$) δ = 11.0, 23.2, 25.5, 42.2, 46.6, 55.3, 70.9, 73.5, 77.6, 78.2, 82.7, 113.7, 113.8, 129.3, 130.3, 130.8, 159.1, 159.2, 179.1; MS *m/z* 426 (M^+, 0.1%), 305 (100); HRMS *m/z* 426.2036 (426.2042 calcd for $C_{25}H_{30}O_6$, M^+). Anal. Found: C, 70.71; H, 7.07%. Calcd for $C_{25}H_{30}O_6$: C, 70.40; H, 7.09%.

(1*R*,2*R*,3*S*,4*S*)-2-{(1*R*)-1-Methylprop-2-en-1-yl}-3,4-di-(4-methoxybenzyl)oxy-cyclohexan-1-ol (24). To a solution of **23** (300 mg, 0.703 mmol) in toluene (6 ml) under Ar at -78 °C was slowly added 1.0 mol dm^{-3} solution of diisobutylaluminium hydride in toluene (1.41 ml, 1.41 mmol). After being stirred at -78 °C for 10 min, the reaction mixture was quenched with water and the products were extracted with EtOAc. The organic layer was successively washed with 1.0 mol dm^{-3} aqueous HCl solution, saturated aqueous $NaHCO_3$ solution, and brine, and then dried. Removal of the solvent gave a crude lactol derivatives (301 mg, 100%) as a white solid, which was used for next reaction without further purification. To a suspension of methyltriphenylphosphonium bromide (2.56 g, 7.17 mmol) in THF (12 ml) under Ar at 0 °C was slowly added 1.69 mol dm^{-3} solution of *n*-butyl lithium in hexane (3.82 ml, 6.46 mmol), and the mixture was stirred at 0 °C for 20 min. To this mixture at 0 °C was added a solution of the crude lactol (301 mg) in THF (12 ml), and the reaction mixture was stirred at 60 °C for 3 h. After cooling, the reaction mixture was quenched with saturated aqueous NH_4Cl solution, and the products were extracted with EtOAc. The organic layer was dried, and concentrated to give a residue, which was chromatographed on a column of silica gel (24 g), with EtOAc-toluene (1:20) as eluent, to afford compound **24** (278 mg, 90%) as a colorless syrup: $[\alpha]_D^{23}$ 16.0 (*c* 1.38, $CHCl_3$); IR γ_{max} (neat) 3460, 1610 cm^{-1}; ^{1}H NMR (270 MHz) δ = 1.15 (d, 3 H, J = 7.3 Hz), 1.30-1.94 (m, 6

H), 2.77 (m, 1 H), 3.48 (ddd, 1 H, J = 4.8, 8.1, 10.6 Hz), 3.74 (dd, 1 H, J = 8.1, 11.0 Hz), 3.79 and 3.80 (3s, each 3 H), 4.09 (m, 1 H), 4.55 (d, 1 H, J = 10.3 Hz), 4.55 and 4.64 (2d, each 1 H, J = 11.0 Hz), 4.96 (d, 1 H, J = 10.3 Hz), 5.02 (ddd, 1 H, J = 1.5, 1.5, 10.3 Hz), 5.09 (ddd, 1 H, J = 1.5, 1.5, 17.2 Hz), 5.96 (ddd, 1 H, J = 7.0, 10.3, 17.2 Hz), 6.85, 6.86, 7.23, and 7.29 (4d, each 2 H, J = 8.8 Hz); ^{13}C NMR (75 MHz in $CDCl_3$) δ = 16.9, 24.3, 31.3, 37.4, 50.4, 55.3, 68.9, 71.3, 74.3, 79.1, 84.1, 113.2, 113.7, 113.8, 129.3, 129.5. 131.0, 131.4, 144.1, 159.0, 159.1; MS *m/z* 426 (M^+, 2%), 305 (81), 197 (37), 137 (100); HRMS *m/z* 426.2415 (426.2406 calcd for $C_{26}H_{34}O_5$, M^+). Anal. Found: C, 72.79; H, 7.98%. Calcd for $C_{26}H_{34}O_5$: C, 73.21; H, 8.03%.

(1*R*,2*S*,3*S*,4*S*)-3-{(1*R*)-1-Methylprop-2-en-1-yl}-4-(*tert*-butyldimethylsilyl)oxy-1,2-di-(4-methoxybenzyl)oxy-cyclohexane (25). To a solution of **24** (41.0 mg, 0.0961 mmol) in CH_2Cl_2 (1 ml) at 0 °C under Ar were added 2,6-lutidine (44.8 μl, 0.384 mmol), and *tert*-butyldimethylsilyl trifluoromethanesulfonate (44.1 μl, 0.192 mmol), and the mixture was stirred at 0 °C for 30 min. The reaction mixture was diluted with CH_2Cl_2, and washed with brine, and then dried. Removal of the solvent gave a residue, which was chromatographed on a column of silica gel (2.5 g), with EtOAc-hexanes (1:10) as eluent, to afford compound **25** (47.8 mg, 92%) as a colorless syrup: $[\alpha]_D^{23}$ 16.1 (*c* 1.12, $CHCl_3$); IR γ_{max} (neat) 1615 cm^{-1}; ^{1}H NMR (270 MHz) δ = 0.05, 0.07 (2s, each 3 H), 0.92 (s, 9 H), 1.11 (d, 3 H, J = 7.3 Hz), 1.29 (m, 1 H), 1.45 (ddd, 1 H, J = 2.0, 5.2, 10.8 Hz), 1.69-1.88 (m, 3 H), 2.71 (m, 1H), 3.45 (ddd, 1 H, J = 5.1, 8.4, 10.4 Hz), 3.70 (dd, 1 H, J = 8.4, 10.8 Hz), 3.79 and 3.80 (2s, each 3 H), 4.08 (m, 1 H), 4.53 (d, 1 H, J = 10.3 Hz), 4.55 and 4.64 (2d, each 1 H, J = 11.4 Hz), 4.94 (ddd, 1 H, J = 1.5, 1.5, 10.4 Hz), 4.96 (d, 1 H, J = 10.3 Hz), 5.00 (ddd, 1 H, J = 1.5, 1.5, 17.2 Hz), 5.97 (ddd, 1 H, J = 6.8, 10.4, 17.2 Hz), 6.84, 6.86, 7.25, and 7.29 (4d, each 2 H, J = 8.8 Hz); ^{13}C NMR (75 MHz in $CDCl_3$) δ = –4.5, –3.7, 16.7, 18.1, 24.6, 26.1, 31.7, 36.7, 51.9, 55.2, 69.1, 71.5, 74.2, 79.7, 84.8, 112.0, 113.7, 113.8, 129.4, 131.1, 131.7, 144.3, 158.9, 159.1; MS *m/z* 540 (M^+, 1%), 419 (5), 137 (18), 121 (100); HRMS *m/z* 540.3270 (540.3271 calcd for $C_{32}H_{48}O_5Si$, M^+). Anal. Found: C, 71.36; H, 9.06%. Calcd for $C_{32}H_{48}O_5Si$: C, 71.07; H, 8.95%.

(3*R*)-3-{(1*S*,2*S*,3*S*,6*R*)-6-(*tert*-Butyldimethylsilyl)oxy-2,3-di-(4-methoxybenzyl)oxy-cyclohex-1-yl}butan-1-ol (26). To a solution of **25** (321 mg, 0.594 mmol) in THF (5 ml) at 0 °C under Ar was added 1.0 mol dm^{-3} solution of borane-tetrahydrofuran complex in THF (1.19 ml, 1.19 mmol), and the mixture was stirred at 0 °C for 2 h. To the reaction mixture were added water (0.8 ml), 3 mol dm^{-3} aqueous NaOH solution (8 ml), and 35% aqueous H_2O_2 solution (8 ml), and the mixture was further stirred at 0 °C for 1 h. The products were extracted with EtOAc and the organic layer was washed with brine, and then dried. Removal of the solvent gave a residue, which was chromatographed on a column of silica gel (25 g), with EtOAc-hexanes (1:2) as eluent, to afford compound **26** (301 mg, 91%) as a colorless syrup: $[\alpha]_D^{21}$ 0.5 (*c* 4.33, $CHCl_3$); IR γ_{max} (neat) 3420, 1615 cm^{-1}; ^{1}H NMR (270 MHz) δ = 0.07, 0.08 (2s, each 3 H), 0.91 (s, 9 H), 1.01 (d, 3 H, J = 7.0 Hz), 1.54-1.95 (m, 8 H), 2.15 (m, 1 H), 3.39-3.83 (m, 4 H), 3.79 and 3.80 (2s, each 3 H), 4.15 (br, 1 H), 4.54 (d, 1 H, J = 10.3 Hz), 4.55 and 4.63 (2d, each 1 H, J = 11.7 Hz), 5.03 (d, 1 H, J = 10.3 Hz), 6.85 (d, 2 H, J = 8.4 Hz), 6.86 and 7.24 (2d, each 2 H, J = 8.8 Hz), 7.29 (d, 2 H, J = 8.4 Hz); ^{13}C NMR (75 MHz in $CDCl_3$) δ = –4.3, –3.6, 17.2, 18.0, 24.6, 26.1, 28.4, 31.9, 38.0, 50.4, 55.2, 61.5, 68.7, 71.5. 74.6, 79.5, 84.7, 113.7, 129.4, 131.0, 131.4, 159.0; MS *m/z* 437 (M^+–PMB, 8%), 283 (6), 137 (9), 121 (100); HRMS *m/z* 437.2726 (437.2723 calcd for $C_{24}H_{41}O_5Si$, M^+–PMB). Anal. Found: C, 68.50; H, 8.95%. Calcd for $C_{32}H_{50}O_6Si$: C, 68.78; H, 9.02%.

(3*R*)-3-{(1*S*,2*S*,3*S*,6*R*)-6-(*tert*-Butyldimethylsilyl)oxy-2,3-di-(4-methoxybenzyl)oxy-cyclohex-1-yl)butanal (27). A mixture of compound **26** (391 mg, 0.770 mmol), molecular sieves powder (4Å, 400 mg), tetrapropylammonium perruthenate (12.3 mg, 0.0350 mmol), and 4-methylmorpholine *N*-oxide (135 mg, 1.16 mmol) in CH_2Cl_2 (8 ml) under Ar was stirred at room temperature for 30 min. Removal of the solvent gave a residue, which was diluted with Et_2O and filtered through Celite. The filtrate was concentrated to give a residue, which was chromatographed on a column of silica gel (40 g), with EtOAc-hexanes (1:6) as eluent, to afford compound **27** (317 mg, 81%) as a colorless syrup: $[\alpha]_D^{20}$ –15.1 (*c* 1.20, $CHCl_3$); IR γ_{max} (neat) 1720, 1615 cm^{-1}; ^{1}H NMR (270 MHz) δ = 0.07 (s, 6 H), 0.90 (s, 9 H), 1.05 (d, 3 H, J = 6.8 Hz), 1.26-1.42 (m, 2 H), 1.69-1.92 (m, 3 H), 2.36 (ddd, 1 H, J = 2.4, 10.2, 15.6 Hz), 2.55 (m, 1 H), 2.72 (m, 1 H), 3.45 (m, 1 H), 3.76 (m, 1 H), 3.80 (s, 6 H), 4.08 (br, 1 H), 4.54 (d, 2 H, J = 10.7 Hz), 4.63 and 5.07 (2d, J = 10.7 Hz, each 1 H), 6.86 (d, 4 H, J = 8.3 Hz), 7.25, 7.29 (2d, each 2 H, J = 8.3 Hz), 9.69 (dd, 1 H, J = 1.5, 2.4 Hz); ^{13}C NMR (75 MHz in $CDCl_3$) δ = –4.5, –3.8, 18.0, 19.0, 24.5, 25.9, 26.0, 28.4, 31.6,

49.3, 50.5, 55.2, 70.3, 71.5, 74.5, 79.8, 84.7, 113.7, 113.8, 129.4, 129.5, 130.9, 131.3, 159.0, 159.1, 203.2; MS *m/z* 435 (M^+–PMB, 19%), 299 (8), 137 (9), 121 (100); HRMS *m/z* 435.2566 (435.2567 calcd for $C_{24}H_{39}O_5Si$, M^+–PMB). Anal. Found: C, 68.79; H, 8.75%. Calcd for $C_{32}H_{48}O_6Si$: C, 69.03; H, 8.69%.

(2*E*)-3-{(1*S*,2*S*,3*S*,6*R*)-6-(*tert*-Butyldimethylsilyl)oxy-2,3-di-(4-methoxybenzyl)oxy-cyclohex-1-yl)but-2-enal (28E) and its (2*Z*)-Isomer (28Z). To a solution of **27** (184 mg, 0.331 mmol) in THF (50 ml) at 0 °C under Ar was slowly added 0.5 mol dm^{-3} solution of potassium bis(trimethylsilyl)amide in toluene (4.97 ml, 2.48 mmol). After being stirred at room temperature for 30 min, a mixture of chlorotrimethylsilane (0.272 ml) and triethylamine (0.277 ml) was added, and the resultant mixture was further stirred at room temperature for 20 min. The reaction was quenched with saturated aqueous $NaHCO_3$ solution, and the products were extracted twice with Et_2O. The combined organic layer was washed with brine, and then dried over Na_2CO_3. Removal of the solvent gave crude silyl enol ether, which was used for next reaction without further purification. A mixture of the crude silyl enol ether, $Pd(OAc)_2$ (81.8 mg, 0.364 mmol) in acetonitrile (5 ml) under Ar was stirred at 0 °C for 12 h. The mixture was diluted with EtOAc and the insoluble material was removed by filtration through Celite, and the filtrate was successively washed with 20% aqueous $Na_2S_2O_3$ solution, saturated aqueous $NaHCO_3$ solution, and brine, and then dried. Removal of the solvent gave a residue, which was chromatographed on a column of silica gel (20 g), with EtOAc-hexanes (1:10) as eluent, to afford first, unchanged starting material compound **27** (12.5 mg, 12%). Further elution gave **28Z** (13.8 mg, 8%) and then **28E** (86.8 mg, 47%), both as a colorless syrup. Compound **28E**: $[\alpha]_D^{22}$ -28.8 (*c* 1.21, $CHCl_3$); IR γ_{max} (neat) 1670, 1615 cm^{-1}; ^1H NMR (270 MHz) δ = –0.08 and 0.00 (2s, each 3 H), 0.88 (s, 9 H), 1.45 (m, 1 H), 1.74-1.90 (m, 3 H), 2.22 (d, 3 H, J = 1.0 Hz), 2.27 (m, 1 H), 3.48 (ddd, 1 H, J = 4.9, 8.3, 10.7 Hz), 3.77 and 3.80 (2s, each 3 H), 3.93 (dd, 1 H, J = 8.5, 11.0 Hz), 3.98 (br, 1 H), 4.46 (d, 1 H, J = 10.7 Hz), 4.55 and 4.64 (2d, each 1 H, J = 11.2 Hz), 4.99 (d, 1 H, J = 10.7 Hz), 5.99 (dd, 1 H, J = 1.0, 7.8 Hz), 6.81, 6.87, 7.11, and 7.29 (4d, each 2 H, J = 8.8 Hz), 10.0 (d, 1 H, J = 7.8 Hz); ^{13}C NMR (75 MHz in $CDCl_3$) δ = –4.9, –4.8, 17.9, 18.2, 24.4, 25.8, 32.0, 55.3, 57.6, 70.9, 71.5, 74.7, 78.5, 83.8, 113.7, 113.8, 113.9, 129.1, 129.5, 130.6, 131.0, 159.0, 159.2, 162.9, 190.9; MS *m/z* 554 (M^+, 1%), 433 (18), 165 (29), 137 (16), 121 (100); HRMS *m/z* 554.3044 (554.3063 calcd for $C_{32}H_{46}O_6Si$, M^+). Anal. Found: C, 69.54; H, 8.27%. Calcd for $C_{32}H_{46}O_6Si$: C, 69.28; H, 8.36%. Compound **28Z**: $[\alpha]_D^{25}$ 22.6 (*c* 1.27, $CHCl_3$); IR γ_{max} (neat) 1675, 1615 cm^{-1}; ^1H NMR (270 MHz) δ = –0.04 and 0.02 (2s, each 3 H), 0.90 (s, 9 H), 1.48-2.03 (m, 4 H), 2.10 (s, 3 H), 3.41 (bd, 1 H, J = 10.7 Hz), 3.55 (ddd, 1 H, J = 4.4, 8.4, 10.9 Hz), 3.77 and 3.81 (2s, each 3 H), 3.99 (dd, 1 H, J = 8.3, 10.7 Hz), 4.05 (m, 1 H), 4.52, 4.53, 4.65, and 5.09 (4d, each 1 H, J = 11.2 Hz), 5.99 (d, 1 H, J = 7.3 Hz), 6.83, 6.88, 7.14, and 7.38 (4d, each 2 H, J = 8.8 Hz), 9.93 (d, 1 H, J = 7.3 Hz); ^{13}C NMR (75 MHz in $CDCl_3$) δ = –5.0, –4.8, 17.9, 24.3, 25.9, 31.8, 55.3, 71.3, 73.8, 83.8, 113.7, 113.9, 128.5, 128.6, 129.2, 129.4, 129.5, 130.5, 131.1, 159.0, 159.2, 189.9; MS *m/z* 554 (M^+, 1%), 433 (23), 297 (22), 165 (58), 137 (28), 121 (100); HRMS *m/z* 554.3060 (554.3063 calcd for $C_{32}H_{46}O_6Si$, M^+).

(2*E*)-3-{(1*S*,2*S*,3*S*,6*R*)-6-(*tert*-Butyldimethylsilyl)oxy-2,3-di-(4-methoxybenzyl)oxy-cyclohex-1-yl)but-2-en-1-ol (29). To a solution of **28E** (53.6 mg, 0.0966 mmol) in toluene (1 ml) under Ar at -78 °C was slowly added 1.0 mol dm^{-3} solution of diisobutylaluminium hydride in toluene (0.193 ml, 0.193 mmol). After being stirred at –78 °C for 15 min, the reaction mixture was quenched with water, and the products were extracted with EtOAc. The organic layer was successively washed with 1.0 mol dm^{-3} aqueous HCl solution, saturated aqueous $NaHCO_3$ solution, and brine, and then dried. Removal of the solvent gave a residue, which was chromatographed on a column of silica gel (5 g), with EtOAc-hexanes (1:4) as eluent, to afford compound **29** (50.0 mg, 93%) as a colorless syrup: $[\alpha]_D^{23}$ –2.8 (*c* 1.21, $CHCl_3$); IR γ_{max} (neat) 3440, 1615 cm^{-1}; ^1H NMR (270 MHz) δ = –0.05 and 0.00 (2s, each 3 H), 0.89 (s, 9 H), 1.33-1.52 (m, 3 H), 1.65-2.00 (m, 2H), 1.75 (s, 3 H), 2.10 (dd, 1 H, J = 2.0, 11.4 Hz), 3.47 (ddd, 1 H, J = 5.1, 8.6, 10.8 Hz), 3.78 and 3.80 (2s, each 3 H), 3.89 (dd, 1 H, J = 8.6, 11.4 Hz), 3.94 (m, 1 H), 4.18 (m, 2 H), 4.50 and 4.56 (2d, each 1 H, J = 11.0 Hz), 4.64 and 4.98 (2d, each 1 H, J = 10.6 Hz), 5.50 (bt, 1 H, J = 6.6 Hz), 6.83, 6.87, 7.18, and 7.30 (4d, each 2 H, J = 8.8 Hz); ^{13}C NMR (75 MHz in $CDCl_3$) δ = –4.9, –4.8, 16.7, 18.0, 24.6, 31.8, 55.2, 56.2, 59.5, 71.4, 71.7, 74.3, 79.1, 84.0, 113.6, 113.8, 126.2, 128.9, 129.4, 130.9, 131.6, 138.2, 158.9, 159.1; MS *m/z* 556 (M^+, 4%), 435 (100), 299 (40), 281 (56), 167 (86); HRMS *m/z* 556.3220 (556.3220 calcd for $C_{32}H_{48}O_6Si$, M^+). Anal. Found: C, 68.93; H, 8.66%. Calcd for $C_{32}H_{48}O_6Si$: C, 69.03 ; H, 8.69%.

(1*S*,2*S*,3*S*,4*R*)-3-{(1*E*)-3-Chloro-1-methylprop-1-en-1-yl}-4-(*tert*-butyldimethylsilyl)oxy-1,2-di-(4-methoxybenzyl)oxy-cyclohexane (30). A solution of **29** (51.0 mg, 0.0916 mmol), collidine (160 μl, 0.550 mmol), lithium chloride (23.3 mg, 0.550 mmol), and methanesulfonyl chloride (46.6 μl, 0.605 mmol) in DMF (1.5 ml) under Ar was stirred at room temperature for 1.5 h. The reaction mixture was diluted with water, and the products were extracted twice with EtOAc. The combined organic layer was successively washed with 1.0 mol dm^{-3} aqueous HCl solution, saturated aqueous $NaHCO_3$ solution, and brine, and then dried. Removal of the solvent gave a residue, which was chromatographed on a column of silica gel (2 g), with EtOAc-hexanes (1:10) as eluent, to afford compound **30** (48.8 mg, 93%) as a colorless syrup: $[\alpha]_D^{24}$ –23.5 (*c* 0.79, $CHCl_3$); IR γ_{max} (neat) 1615 cm^{-1}; ^1H NMR (270 MHz) δ = –0.03 and 0.01 (2s, each 3 H), 0.89 (s, 9 H), 1.40 (m, 1 H), 1.68-1.92 (m, 3 H), 1.81 (d, 3 H, J = 1.1 Hz), 2.14 (dd, 1 H, J = 2.2, 11.4 Hz), 3.46 (ddd, 1 H, J = 5.1, 8.6, 10.8 Hz), 3.78 and 3.80 (2s, each 3 H), 3.89 (dd, 1 H, J = 8.6, 11.4 Hz), 3.93 (m, 1 H), 4.15 (m, 2 H), 4.52 (d, 1 H, J = 10.4 Hz), 4.56 and 4.64 (2d,each 1 H, J = 11.0 Hz), 4.95 (d, 1 H, J = 10.4 Hz), 5.59 (bt, 1 H, J = 6.6 Hz), 6.82, 6.87, 7.20, and 7.30 (4d, each 2 H, J = 8.8 Hz); ^{13}C NMR (75 MHz in $CDCl_3$) δ = –4.7, –4.6, 16.7, 18.1, 24.7, 26.1, 32.0, 41.0, 55.4, 56.5, 71.6, 71.8, 74.6, 79.1, 84.1, 113.7, 113.9, 122.9, 129.3, 129.6, 131.0, 131.6, 142.2, 159.1, 159.2; MS *m/z* 576 ($M(^{37}Cl)^+$, 0.1%), 574 (M^+, 0.3%), 455 (12), 453 (30), 317 (9), 185 (16), 149 (20), 137 (24), 121 (100); HRMS *m/z* 574.2880 (574.2881 calcd for $C_{32}H_{47}O_5ClSi$, M^+).

(1*S*,2*S*,3*S*,4*R*)-3-{(1*E*)-1,5-Dimethylhexa-1,4-dien-1-yl}-4-(*tert*-butyldimethylsilyl)oxy-1,2-di-(4-methoxybenzyl)oxy-cyclohexane (32). A mixture of **30** (6.6 mg, 0.0115 mmol), tetrakis(triphenylphosphine)palladium(0) (1.3 mg, 1.15 μmol), and tributylisobutenyltin (**31**) (11.9 mg, 0.0344 mmol) in THF (1 ml) under Ar was stirred at 40 °C for 6 days. The reaction mixture was concentrated to give a residue, which was chromatographed on a column of silica gel (1 g), with EtOAc-hexanes (1:40) as eluent, to afford compound **31** (4.1 mg, 60%) as a colorless syrup: $[\alpha]_D^{25}$ 2.1 (*c* 0.92, $CHCl_3$); IR γ_{max} (neat) 1615 cm^{-1}; ^1H NMR (270 MHz) δ = –0.04 and –0.01 (2s, each 3 H), 0.89 (s, 9 H), 1.26-1.43 (m, 2 H), 1.63, 1.67, and 1.72 (3s, each 3 H), 1.78-1.88 (m, 2 H), 2.20 (dd, 1 H, J = 2.2, 11.2 Hz), 2.74 (bt, 2 H, J = 7.3 Hz), 3.45 (m, 1 H), 3.78 and 3.80 (2s, each 3 H), 3.87 (m, 1 H), 3.91 (m, 1 H), 4.48 (d, 1 H, J = 10.3 Hz), 4.56 and 4.64 (2d, each 1 H, J = 11.0 Hz), 4.91 (d, 1 H, J = 10.3 Hz), 5.14 (tq, 1 H, J = 1.5, 7.3 Hz) 5.27 (bt, 1 H, J = 7.3 Hz), 6.81, 6.87, 7.18, and 7.31 (4d, each 2 H, J = 8.8 Hz); ^{13}C NMR (75 MHz in $CDCl_3$) δ = –5.0, –4.8, 16.7, 17.7, 18.0, 24.7, 25.7, 25.9, 26.1, 27.1, 31.9, 55.3, 56.3, 71.5, 72.1, 74.3, 79.4, 84.1, 113.6, 113.8, 123.3, 125.9, 129.1, 129.2, 129.4, 131.0, 131.1, 131.8, 133.9, 144.4, 158.8, 159.1; MS *m/z* 594 (M^+, 2%), 509 (7), 473 (20), 419 (15), 337 (7), 283 (15), 137 (24), 121 (100); HRMS *m/z* 594.3739 (594.3740 calcd for $C_{36}H_{54}O_5Si$, M^+).

(1*R*,2*R*,3*S*,4*S*)-2-{(1*E*)-1,5-Dimethylhexa-1,4-dien-1-yl}-1,2-di-(4-methoxybenzyl)oxy-cyclohexan-1-ol (33). To a solution of **32** (19.8 mg, 0.0333 mmol) in THF (1 ml) at room temperature was added 1.0 mol dm^{-3} solution of tetra-*n*-butylammonium fluoride in THF (0.333 ml, 0.333 mmol), and the mixture was stirred at room temperature for 7 days. The reaction mixture was concentrated to give a residue, which was chromatographed on a column of silica gel (1.6 g), with EtOAc-hexanes (1:4) as eluent, to afford compound **33** (13.4 mg, 84%) as a colorless syrup: $[\alpha]_D^{28}$ –35.4 (*c* 0.64, $CHCl_3$); IR γ_{max} (neat) 3460, 1615 cm^{-1}; ^1H NMR (270 MHz) δ = 1.64 (s, 3 H), 1.66 (d, 3 H, J = 1.0 Hz), 1.75 (s, 3 H), 1.34-2.00 (m, 4 H), 2.18 (dd, 1 H, J = 2.2, 11.2 Hz), 2.70 (bt, 2 H, J = 7.0 Hz), 3.45 (ddd, 1 H, J = 4.4, 8.6, 11.2 Hz), 3.78 and 3.80 (2s, each 3 H), 3.76-3.83 (m, 2 H), 4.46 (d, 1 H, J = 10.3 Hz), 4.57 and 4.65 (2d, each 1 H, J = 11.0 Hz), 4.88 (d, 1 H, J = 10.3 Hz), 5.12 (tq, 1 H, J = 1.0, 7.0 Hz), 5.36 (bt, 1 H, J = 7.0 Hz), 6.82, 6.87, 7.17, and 7.33 (4d, each 2 H, J = 8.8 Hz); ^{13}C NMR (75 MHz in $CDCl_3$) δ = 17.7, 18.2, 24.6, 25.6, 27.1, 29.6, 55.3, 55.9, 67.2, 71.3, 75.0, 78.7, 83.9, 113.6, 113.7, 122.7, 125.0, 129.2, 129.4, 131.2, 131.5, 133.5, 142.7, 158.9, 159.0; MS *m/z* 480 (M^+, 1%), 359 (33), 205 (7), 137 (21), 121 (100); HRMS *m/z* 480.2878 (480.2875 calcd for $C_{30}H_{40}O_5$, M^+).

(1*R*,2*R*,3*S*,4*S*)-2-[(2*R*,3*S*)-3-(3-Methyl-2-buten-1-yl)-2-methyloxiran-2-yl]-3,4-di-(4-methoxybenzyl)oxy-cyclohexan-1-ol (34). To a solution of **33** (5.1 mg, 0.0106 mmol) and vanadyl acetylacetonate (0.3 mg, 1.06 μmol) in CH_2Cl_2 (1 ml) at –10 °C under Ar was added 5.0-6.0 mol dm^{-3} solution of *tert*-butyl hydroperoxide in decane (3.1 ml, 0.0155-0.0186 mmol), and the mixture was stirred at -8 °C for 5 h. To the reaction mixture was added dimethyl sulfide (0.1 ml), and the mixture was further stirred at 0 °C for 30 min. The reaction mixture was concentrated to give a residue, which was chromatographed on a column of

silica gel (1 g), with EtOAc-hexanes (1:4) as eluent, to afford compound **34** (4.8 mg, 91%) as a colorless syrup: $[\alpha]_D^{27}$ 37.9 (*c* 0.30, $CHCl_3$); IR γ_{max} (neat) 3470, 1615 cm^{-1}; ^1H NMR (270 MHz) δ = 1.43 and 1.56 (2s, each 3 H), 1.61 (d, 3 H, J = 1.1 Hz), 1.75 (s, 3 H), 1.65-1.95 (m, 4 H), 2.29 (m, 1 H), 3.09 (bt, 1 H, J = 6.2 Hz), 3.37 and 3.43 (2m, each 1 H), 3.65 (dd, 1 H, J = 8.4, 11.0 Hz), 3.78 and 3.80 (2s, each 3 H), 4.27 (m, 1 H), 4.48, 4.51, 4.61, and 5.05 (4d, each 1 H, J = 11.0 Hz), 5.14 (m, 1 H), 6.84 (d, 2 H, J = 8.8 Hz), 6.85 (d, 2 H, J = 8.4 Hz), 7.20 (d, 2 H, J = 8.8 Hz), 7.25 (d, 2 H, J = 8.4 Hz); ^{13}C NMR (75 MHz in $CDCl_3$) δ = 17.9, 21.1, 24.3, 25.6, 27.5, 30.2, 50.9, 55.3, 61.4, 64.1, 68.1, 71.1, 73.9, 77.2, 78.9, 84.1, 113.7, 118.8, 128.7, 129.3, 129.6, 130.9, 131.5, 134.6, 158.9, 159.1; MS *m/z* 496 (M^+, 0.3%), 375 (16), 305 (12), 289 (13), 221 (14), 151 (21), 137 (77), 121 (100); HRMS *m/z* 496.2829 (496.2824 calcd for $C_{30}H_{40}O_6$, M^+).

(2*R*,3*S*,4*S*)-2-[(2*R*,3*S*)-3-(3-Methy-2-buten-1-yl)-2-methyloxiran-2-yl]-3,4-di-(4-methoxybenzyl)oxy-cyclohexan-1-one (35). A suspension of compound **34** (4.8 mg, 9.7 mmol), pyridinium dichromate (10.9 mg, 29.0 mmol), and molecular sieves powder (4 Å, 10 mg) in CH_2Cl_2 (1 ml) was stirred at 0 °C for 22 h. The mixture was diluted with Et_2O and insoluble material was removed by filtration through a short pad of silica gel. The filtrate was concentrated to give a residue, which was chromatographed on a column of silica gel (1.2 g), with EtOAc-hexanes (1:4) as eluent, to afford **35** (2.9 mg, 60 %) as a colorless syrup: $[\alpha]_D^{26}$ 47.3 (*c* 0.15, $CHCl_3$); IR γ_{max} (neat) 1715, 1615, 1515 cm^{-1}; ^1H NMR (270 MHz) δ = 1.26 (s, 3 H), 1.65 and 1.74 (2d, each 3 H, J = 1.5 Hz), 2.17-2.43 (m, 6 H), 2.26 (d, 1 H, J = 8.8 Hz), 2.57 (dd, 1 H, J = 6.2, 6.2 Hz), 3.80 and 3.81 (2s, each 3 H), 3.82 (m, 1 H), 3.89 (dd, 1 H, J = 6.8, 8.8 Hz), 4.57 and 4.61 (2d, each 1 H, J = 11.4 Hz), 4.71 and 4.81 (2d, each 1 H, J = 10.5 Hz), 5.31 (dddd, 1 H, J = 1.5, 1.5, 7.1, 7.1 Hz), 6.86, 6.87, 7.25, and 7.35 (4d, each 2 H, J = 8.7 Hz); ^{13}C NMR (75 MHz in $CDCl_3$) δ = 14.3, 18.0, 24.7, 25.7, 27.8, 37.2, 55.3, 58.5, 62.4, 63.3, 71.4, 72.8, 77.2, 78.9, 79.9, 113.7, 113.8, 119.0, 129.3, 129.6, 130.2, 130.5, 134.0, 159.3, 206.8; MS *m/z* 476 (M^+-H_2O, 1%), 355 (1), 202 (3), 137 (16), 121 (100); HRMS *m/z* 476.2561 (476.2563 calcd for $C_{30}H_{36}O_5$, M^+-H_2O).

(2*S*,3*S*,4*S*)-2-{(1*E*)-1,5-Dimethylhexa-1,4-dien-1-yl}-3,4-di-(4-methoxybenzyl)oxy-cyclohexan-1-one (37). A solution of compound **33** (6.0 mg, 0.0125 mmol) in acetic anhydride (0.4 ml) and DMSO (0.6 ml) was stirred at room temperature for 18 h. To the reaction mixture was added EtOH (1 ml). After being stirred at room temperature for 30 min, the mixture was diluted with EtOAc, and washed three times with water, and then dried. Removal of the solvent gave a residue, which was chromatographed on a column of silica gel (1 g), with EtOAc-hexanes (1:8) as eluent, to afford compound **37** (3.8 mg, 63%) as a colorless syrup: $[\alpha]_D^{26}$ 71.9 (*c* 0.35, $CHCl_3$); IR γ_{max} (neat) 1715, 1615, 1515 cm^{-1}; ^1H NMR (270 MHz) δ = 1.59 (m, 1 H), 1.63, 1.64, and 1.69 (3d, each 3 H, J = 1.2 Hz), 2.15-2.46 (m, 2 H), 2.80 (m, 2 H), 3.06 (d, 1 H, J = 10.3 Hz), 3.68 (dd, 1 H, J = 8.1, 10.3 Hz), 3.80 and 3.82 (2s, each 3 H), 4.48 (d, 1 H, J = 10.3 Hz), 4.66 (s, 2 H), 4.73 (d, 1 H, J = 10.3 Hz), 5.14 (dddd, 1 H, J = 1.2, 1.2, 7.2, 7.2 Hz), 5.25 (ddd, 1 H, J = 1.2, 7.2, 7.2 Hz), 6.83 (d, 2 H, J = 8.8 Hz), 6.89 (d, 2 H, J = 8.5 Hz), 7.20 (d, 2 H, J = 8.8 Hz), 7.30 (d, 2 H, J = 8.5 Hz); ^{13}C NMR (75 MHz in $CDCl_3$) δ = 14.4, 17.8, 25.6, 27.3, 38.0, 55.1, 55.4, 65.3, 65.5, 71.9, 74.1, 80.5, 81.2, 113.7, 113.8, 122.4, 122.6, 129.1, 129.4, 129.7, 130.2, 130.5, 130.6, 159.2, 207.7; MS *m/z* 478 (M^+, 0.2%), 357 (1), 236 (3), 204 (3), 137 (7), 121 (100); HRMS *m/z* 478.2717 (478.2719 calcd for $C_{30}H_{38}O_5$, M^+).

(4*S*,5*S*,6*S*)-4-{(1*E*)-1,5-Dimethylhexa-1,4-dien-1-yl}-5,6-di-(4-methoxybenzyl)-1-oxaspiro[2.5]octane (38). A solution of trimethylsulfoxonium iodide (95.2 mg, 0.432 mmol) and sodium hydride (6.9 mg, 0.288 mmol) in DMSO (0.6 ml) under Ar was stirred at room temperature for 1 h. To this mixture was slowly added a solution of compound **37** (6.9 mg, 0.0144 mmol) in DMSO (0.3 ml). After being stirred for 30 min, the reaction mixture was quenched with a buffer solution (pH = 7, prepared from 0.2 mol dm^{-3} aqueous NaH_2PO_4 solution and 0.2 mol dm^{-3} aqueous NaOH solution), and the products were extracted with EtOAc. The organic layer was dried and concentrated to give a residue, which was chromatographed on a column of silica gel (1 g), with EtOAc-hexanes (1:10) as eluent, to afford compound **38** (3.3 mg, 47%) as a colorless syrup: $[\alpha]_D^{25}$ 8.6 (*c* 0.17, $CHCl_3$); IR γ_{max} (neat) 1615, 1515 cm^{-1}; ^1H NMR (270 MHz) δ = 1.26 (m, 1 H), 1.62, 1.63, and 1.68 (3d, each 3 H, J = 1.2 Hz), 1.71-1.91 (m, 2 H), 2.07 (m, 1 H), 2.47 (d, 1 H, J = 5.0 Hz), 2.53 (d, 1 H, J = 11.0 Hz), 2.61 (d, 1 H, J = 5.0 Hz), 2.73 (dd, 2 H, J = 6.0, 7.1 Hz), 3.54 (ddd, 1 H, J = 4.4, 8.5, 11.2 Hz), 3.75 (dd, 1 H, J = 8.5, 11.0 Hz), 3.79 and 3.81 (2s, each 3 H), 4.47 (d, 1 H, J = 10.4 Hz), 4.60 and 4.66 (2d, each 1 H, J = 11.2 Hz), 4.98 (d, 1 H, J = 10.4 Hz), 5.10 (ddt, 1 H, J =

1.2, 1.2, 7.1 Hz), 5.29 (dt, 1 H, J = 1.2, 6.0 Hz), 6.83, 6.87, 7.16, and 7.30 (4d, each 2 H, J = 8.8 Hz); ^{13}C NMR (75 MHz in $CDCl_3$) δ = 15.3, 17.7, 25.7, 27.1, 31.8, 50.5, 53.7, 55.1, 55.5, 59.9, 71.6, 81.8, 82.8, 83.0, 113.6, 113.7, 122.7, 129.3, 130.8, 131.0, 131.4, 159.0, 159.1; MS *m/z* 492 (M^+, 0.2%), 371 (7), 137 (14), 121 (100); HRMS *m/z* 492.2878 (492.2875 calcd for $C_{31}H_{40}O_5$, M^+).

(1*R*,2*R*,3*S*,4*S*)-2-{(1*E*)-1-Methylprop-1-en-1-yl)-3,4-di-(4-methoxybenzyl)oxy-cyclohexan-1-ol (40). A solution of compound **24** (76.3 mg, 0.179 mmol) and chlorotris(triphenylphosphine)rhodium(I) (82.8 mg, 0.0894 mmol) in EtOH (1 ml) and benzene (3 ml) under Ar in a sealed tube was stirred at 120 °C for 2 days. After cooling, the reaction mixture was concentrated to give a residue, which was chromatographed on a column of silica gel (8 g), with EtOAc-toluene (1:8) as eluent, to afford compound **40** (65.3 mg, 86 %) as a colorless syrup: $[\alpha]_D^{27}$ 8.4 (*c* 1.03, $CHCl_3$); IR γ_{max} (neat) 3460, 1615, 1515 cm^{-1}; ^1H NMR (270 MHz) δ = 1.35-2.00 (m, 4 H), 1.70 (d, 3 H, J = 7.3 Hz), 1.72 (d, 3 H, J = 1.5 Hz), 2.17 (dd, 1 H, J = 1.5, 11.4 Hz), 3.46 (ddd, 1 H, J = 4.8, 8.8, 11.4 Hz), 3.79 (s, 3 H), 3.80 (m, 2 H), 3.81 (s, 3 H), 4.47 (d, 1 H, J = 10.3 Hz), 4.56 and 4.65 (2d, each 1 H, J = 11.3 Hz), 4.89 (d, 1 H, J = 10.3 Hz), 5.41 (m, 1 H), 6.83, 6.87, 7.16, and 7.30 (4d, each 2 H, J = 8.8 Hz); ^{13}C NMR (75 MHz in $CDCl_3$) δ = 13.4, 17.8, 25.6, 29.6, 55.3, 55.9, 67.3, 71.3, 74.9, 78.9, 84.0, 113.6, 113.8, 120.1, 128.8, 129.3, 129.5, 131.2, 131.6, 134.6, 159.0; MS *m/z* 426 (M^+, 3%), 305 (100); HRMS *m/z* 426.2407 (426.2406 calcd for $C_{26}H_{34}O_5$, M^+).

(1*R*,2*R*,3*S*,4*S*)-2-{(2*R*,3*S*)- (41a) and (1*R*,2*R*,3*S*,4*S*)-2-{(2*S*,3*R*)-2,3-Dimethyloxiran-2-yl}-3,4-di-(4-methoxybenzyl)oxy-cyclohexan-1-ol (41b). To a solution of **40** (62.0 mg, 0.145 mmol), vanadyl acetylacetonate (1.9 mg, 7.3 μmol) in benzene (1 ml) under Ar at -15 °C was added 5.0-6.0 mol dm^{-3} solution of *tert*-butyl hydroperoxide in decane (43.6 μl, 0.218-0.262 mmol), and the mixture was stirred at −15 °C for 4 h. To the reaction mixture was added dimethyl sulfide (0.1 ml), and the mixture was further stirred at −10 °C for 30 min. The reaction mixture was concentrated to give a residue, which was chromatographed on a column of silica gel (6 g), with EtOAc-hexanes (1:5 → 1:2) as eluent, to afford first, compound **41a** (44.0 mg, 68%) as needles. Further elution gave compound **41b** (7.7 mg, 12%) as a colorless syrup. Compound **41a**: M.p. 98-99 °C (from MeOH); $[\alpha]_D^{20}$ −15.5 (*c* 1.07, $CHCl_3$); IR γ_{max} (KBr) 3415, 1615, 1515 cm^{-1}; ^1H NMR (270 MHz) δ = 1.25 (d, 3 H, J = 5.5 Hz), 1.35 (m, 1 H), 1.37 (s, 3 H), 1.74 (dd, 1 H, J = 2.0, 11.1 Hz), 1.76-1.90 (m, 3 H), 3.18 (q, 1 H, J = 5.5 Hz), 3.44 (ddd, 1 H, J = 4.6, 8.4, 13.4 Hz), 3.48 (m, 1 H), 3.63 (dd, 1 H, J = 8.4, 11.1 Hz), 3.80 (s, 6 H), 4.28 (m, 1 H), 4.46 (d, 1 H, J = 10.7 Hz), 4.51 and 4.63 (2d, each 1 H, J = 11.0 Hz), 5.04 (d, 1 H, J = 10.7 Hz), 6.86, 6.87, 7.21, and 7.28 (4d, each 2 H, J = 8.7 Hz); ^{13}C NMR (75 MHz in $CDCl_3$) δ = 13.6, 20.8, 24.4, 30.1, 50.7, 55.2, 57.4, 63.9, 68.1, 71.1, 74.3, 79.1, 84.0, 113.7, 129.0, 129.3, 130.9, 131.3, 159.0, 159.1; MS *m/z* 442 (M^+, 1%), 424 (7), 321 (100), 305 (18), 242 (84), 235 (100); HRMS *m/z* 442.2355 (442.2355 calcd for $C_{26}H_{34}O_6$, M^+). Compound **41b**: $[\alpha]_D^{28}$ 12.8 (*c* 1.27, $CHCl_3$); IR γ_{max} (neat) 3440, 1615, 1515 cm^{-1}; ^1H NMR (270 MHz) δ = 1.34 (d, 3 H, J = 5.9 Hz), 1.45 (s, 3 H), 1.50-2.00 (m, 4 H), 1.63 (dd, 1 H, J = 2.0, 11.0 Hz), 2.84 (q, 1 H, J = 5.9 Hz), 3.50 (ddd, 1 H, J = 4.4, 8.4, 10.6 Hz), 3.78 and 3.81 (2s, each 3 H), 3.95 (dd, 1 H, J = 8.4, 11.0 Hz), 4.15 (m, 1 H), 4.57 and 4.64 (2d, each 1 H, J = 11.2 Hz), 4.67 and 5.08 (2d, each 1 H, J = 10.8 Hz), 6.87, 6.88, 7.31, and 7.36 (4d, each 2 H, J = 8.8 Hz); ^{13}C NMR (75 MHz in $CDCl_3$) δ = 14.4, 24.4, 31.8, 49.7, 55.2, 55.3, 58.5, 61.6, 68.6, 71.4, 74.0, 78.2, 83.7, 113.6, 113.8, 129.0, 129.4, 130.8, 131.5, 158.8, 159.1; MS *m/z* 442 (M^+, 2%), 424 (15), 321 (100), 305 (28), 185 (70), 167 (100); HRMS *m/z* 442.2355 (442.2355 calcd for $C_{26}H_{34}O_6$, M^+).

(1*R*,2*R*,3*S*,4*S*)-2-{(1*E*)-3-Hydroxy-1-methylprop-1-en-1-yl}-3,4-di-(4-methoxybenzyl)oxy-cyclohexan-1-ol (42). To a solution of **29** (83.6 mg, 0.150 mmol) in THF (1.5 ml) at room temperature was added 1.0 mol dm^{-3} solution of tetra-*n*-butylammonium fluoride in THF (1.50 ml, 1.50 mmol), and the mixture was stirred at room temperature for 6 days. The reaction mixture was concentrated to give a residue, which was chromatographed on a column of silica gel (3 g), with EtOAc-toluene (1:1) as eluent, to afford compound **42** (66.4 mg, 100%) as a colorless syrup: $[\alpha]_D^{17}$ −14.7 (*c* 0.73, $CHCl_3$); IR γ_{max} (neat) 3390, 1615, 1515 cm^{-1}; ^1H NMR (270 MHz) δ = 1.43 (m, 1 H), 1.74-2.10 (m, 4 H), 1.77 (s, 3 H), 2.15 (dd, 1 H, J = 2.0, 11.2), 2.35 (br, 1 H), 3.47 (ddd, 1 H, J = 4.4, 8.5, 11.2 Hz), 3.78 and 3.80 (2s, each 3 H), 3.79-3.86 (m, 2 H), 4.17 (dd, 1 H, J = 6.6, 12.5 Hz), 4.23 (dd, 1 H, J = 6.8, 12.5 Hz), 4.50 (d, 1 H, J = 10.6 Hz), 4.56 and 4.65 (2d, each 1 H, J = 11.0 Hz), 4.93 (d, 1 H, J = 10.6 Hz), 5.53 (dd, 1 H, J = 6.6, 6.8 Hz), 6.82, 6.87, 7.17, and 7.30 (4d, each 2 H, J = 8.8 Hz); ^{13}C NMR (75 MHz in $CDCl_3$) δ = 18.1, 24.5, 30.1, 55.2, 55.7, 59.0, 67.7, 71.3, 74.8, 78.8, 83.8, 113.6, 113.7, 125.1, 129.2, 129.3, 131.0, 131.4, 137.9, 159.0;

MS *m/z* 442 (M^+, 1%), 424 (2), 321 (100), 303 (56), 167 (70), 149 (82); HRMS *m/z* 442.2356 (442.2355 calcd for $C_{26}H_{34}O_6$, M^+).

(1*R*,2*R*,3*S*,4*S*)-2-{(1*E*)-3-(*tert*-Butyldimethylsilyl)oxy-1-methylprop-1-en-1-yl}-3,4-di-(4-methoxybenzyl)oxy-cyclohexan-1-ol (43). To a solution of compound **42** (86.7 mg, 0.196 mmol) in DMF (2 ml) at 0 °C was added imidazole (80.1 mg, 1.18 mmol) and *tert*-butyldimethylsilyl chloride (88.6 mg, 0.588 mmol), and the mixture was stirred at room temperature for 30 min. The reaction mixture was diluted with EtOAc and washed with water, and dried. Removal of the solvent left a residue, which was chromatographed on a column of silica gel (4 g), with EtOAc-hexanes (1:4) as eluent, to afford compound **43** (96.9 mg, 89%) as a colorless syrup: $[\alpha]_D^{23}$ –20.0 (*c* 1.19, $CHCl_3$); IR γ_{max} (neat) 3450, 1615, 1515 cm^{-1}; ^1H NMR (270 MHz) δ = 0.06 (s, 6 H), 0.88 (s, 9 H), 1.43 (m, 1 H), 1.74 (s, 3 H), 1.77-2.00 (m, 3 H), 2.17 (dd, 1 H, J = 2.0, 11.2), 3.46 (ddd, 1 H, J = 4.5, 8.8, 13.2 Hz), 3.78 and 3.80 (2s, each 3 H), 3.79-3.87 (m, 2 H), 4.26 (dd, 1 H, J = 5.9, 12.7 Hz), 4.32 (dd, 1 H, J = 6.1, 12.7 Hz), 4.50 (d, 1 H, J = 10.3 Hz), 4.56 (d, 1 H, J = 11.0 Hz), 4.65 (d, 1 H, J = 11.0 Hz), 4.91 (d, 1 H, J = 10.3 Hz), 5.55 (dd, 1 H, J = 5.9, 6.1 Hz), 6.82, 6.87, 7.18, and 7.30 (4d, each 2 H, J = 8.8 Hz); ^{13}C NMR (75 MHz in $CDCl_3$) δ = –5.2, 18.3, 24.5, 25.9, 29.7, 55.2, 55.8, 60.0, 67.4, 71.3, 75.0, 78.8, 83.8, 113.6, 113.7, 126.4, 129.2, 129.3, 131.0, 131.4, 135.3, 158.9, 159.0; MS *m/z* 556 (M^+, 0.2%), 435 (26), 281 (3), 167 (8), 149 (7), 137 (13), 121 (100); HRMS *m/z* 556.3222 (556.3220 calcd for $C_{32}H_{48}O_6Si$, M^+). Anal. Found: C, 69.02; H, 8.63%. Calcd for $C_{32}H_{48}O_6Si$: C, 69.03; H, 8.69%.

(2*S*,3*S*,4*S*)-2-{(1*E*)-3-(*tert*-Butyldimethylsilyl)oxy-1-methylprop-1-en-1-yl}-3,4-di-(4-methoxybenzyl)oxy-cyclohexan-1-one (44). A solution of compound **43** (48.4 mg, 0.0869 mmol) in acetic anhydride (0.8 ml) and DMSO (1.2 ml) was stirred at room temperature for 12 h. To the reaction mixture was added EtOH (4 ml), and the mixture was further stirred at room temperature for 30 min. The mixture was diluted with EtOAc and washed three times with water, and then dried. Removal of the solvent gave a residue, which was chromatographed on a column of silica gel (2 g), with EtOAc-hexanes (1:5) as eluent, to afford compound **44** (44.8 mg, 93%) as a colorless syrup: $[\alpha]_D^{23}$ 53.7 (*c* 1.06, $CHCl_3$); IR γ_{max} (neat) 1720, 1615, 1515 cm^{-1}; ^1H NMR (270 MHz) δ = 0.07 and 0.08 (2s, each 3 H), 0.90 (s, 9 H), 1.58 (d, 3 H, J = 1.2 Hz), 1.63 (m, 1 H), 2.16-2.45 (m, 3 H), 3.09 (1 H, d, J = 10.1 Hz), 3.69 (dd, 1 H, J = 7.8, 10.1 Hz), 3.79 and 3.81 (2s, each 3 H), 3.81 (m, 1 H), 4.28 (d, 2 H, J = 6.1 Hz), 4.51 (d, 1 H, J = 10.4 Hz), 4.65 (s, 2 H), 4.72 (d, 1 H, J = 10.4 Hz), 5.43 (dt, 1 H, J = 1.2, 6.1 Hz), 6.83, 6.89, 7.22, and 7.29 (4d, each 2 H, J = 8.8 Hz); ^{13}C NMR (75 MHz in $CDCl_3$) δ = –5.2, 14.7, 18.3, 25.5, 25.9, 37.8, 55.2, 55.3, 60.1, 65.0, 71.9, 73.9, 80.3, 81.0, 113.7, 113.8, 129.3, 129.7, 130.4, 130.4, 131.2, 159.2, 207.1; MS *m/z* 554 (M^+, 2%), 497 (37), 433 (100), 359 (53), 297 (52), 280 (100); HRMS *m/z* 554.3084 (554.3063 calcd for $C_{32}H_{46}O_6Si$, M^+).

(2*E*)-3-{(3*R*,4*S*,5*S*,6*S*)-5,6-Di-(4-methoxybenzyl)oxy-1-oxaspiro[2.5]oct-4-yl}-1-(*tert*-butyldimethylsilyl)oxybut-2-ene (45). A solution of trimethylsulfoxonium iodide (252 mg, 1.14 mmol) and sodium hydride (60% in oil, 30.5 mg, 0.763 mmol) in DMSO (1.5 ml) under Ar was stirred at room temperature for 70 min. To this mixture at 18 °C was slowly added a solution of compound **44** (27.2 mg, 0.0508 mmol) in DMSO (1 ml). After being stirred for 15 min, the reaction mixture was quenched with a buffer solution (pH = 7, prepared from 0.2 mol dm^{-3} aqueous NaH_2PO_4 solution and 0.2 mol dm^{-3} aqueous NaOH solution), and the products were extracted with EtOAc. The organic layer was washed with water and brine, and then dried. Removal of the solvent gave a residue, which was chromatographed on a column of silica gel (8 g), with EtOAc-hexanes (1:10) as eluent, to afford compound **45** (16.3 mg, 58%) as a colorless syrup: $[\alpha]_D^{25}$ 4.3 (*c* 0.89, $CHCl_3$); IR γ_{max} (neat) 1615, 1515 cm^{-1}; ^1H NMR (270 MHz) δ = 0.06 (s, 6 H), 0.89 (s, 9 H), 1.26 (ddd, 1 H, J = 3.1, 3.1, 13.9 Hz), 1.58 (s, 3 H), 1.71 (m, 1 H), 1.84 (ddd, 1 H, J = 3.1, 13.9, 13.9 Hz), 2.09 (m, 1 H), 2.48 (d, 1 H, J = 4.9 Hz), 2.56 (d, 1 H, J = 11.0 Hz), 2.63 (d, 1 H, J = 4.9 Hz), 3.55 (ddd, 1 H, J = 4.5, 8.6, 13.1 Hz), 3.76 (dd, 1 H, J = 8.6, 11.0 Hz), 3.79 and 3.81 (2s, each 3 H), 4.19 (dd, 1 H, J = 5.6, 13.1 Hz), 4.25 (dd, 1 H, J = 5.6, 13.1 Hz), 4.48 (d, 1 H, J = 10.5 Hz), 4.60 (d, 1 H, J = 11.0 Hz), 4.66 (d, 1 H, J = 11.0 Hz), 4.87 (d, 1 H, J = 10.5 Hz), 5.47 (dd, 1 H, J = 5.6, 5.6 Hz), 6.82, 6.88, 7.17, and 7.31 (4d, each 2 H, J = 8.8 Hz); ^{13}C NMR (75 MHz in $CDCl_3$) δ = –5.2, 15.7, 18.3, 25.9, 27.0, 29.7, 31.8, 50.4, 53.4, 55.3, 59.7, 60.0, 71.6, 74.5, 81.6, 82.8, 113.6, 113.8, 129.3, 130.5, 131.0, 131.4, 132.2, 159.0, 159.1; MS *m/z* 447 (M^+–PMB, 22%), 137 (7), 121 (100); HRMS *m/z* 447.2563 (447.2567 calcd for $C_{25}H_{39}O_5Si$, M^+–PMB). Anal. Found: C, 69.40; H, 8.28%. Calcd for $C_{33}H_{48}O_6Si$: C, 69.68; H, 8.51%.

(3*R*,4*S*,5*S*,6*S*)-4-{(1*E*)-3-(*tert*-Butyldimethylsilyl)oxy-1-methylprop-1-en-1-yl}-5,6-dihydroxy-1-oxaspiro[2.5]octane (46). To a solution of compound **45** (14.7 mg, 0.0258 mmol) in CH_2Cl_2 (0.45 ml) and water (25 μl) at room temperature was added 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (12.9 mg, 0.0569 mmol), and the mixture was stirred at room temperature for 1 h. The reaction mixture was diluted with saturated aqueous $NaHCO_3$ solution, and the products were extracted with EtOAc. The organic layer was washed four times with saturated aqueous $NaHCO_3$ solution, and then dried. Removal of the solvent gave a residue, which was chromatographed on a column of silica gel (1 g), with EtOAc-hexanes (1:1) as eluent, to afford compound **46** (8.5 mg, 100%) as a colorless syrup: $[\alpha]_D^{22}$ –43.3 (*c* 0.89, $CHCl_3$); IR γ_{max} (neat) 3400 cm^{-1}; ^1H NMR (270 MHz) δ = 0.08 (s, 6 H), 0.90 (s, 9 H), 1.29 (m, 1 H), 1.64 (d, 3 H, J = 1.1 Hz), 1.81-2.10 (m, 4 H), 2.41 (d, 1 H, J = 10.6 Hz), 2.49 (d, 1 H, J = 4.8 Hz), 2.58 (d, 1 H, J = 4.8 Hz), 2.74 (br, 1 H), 3.60 (ddd, 1 H, J = 4.0, 8.8, 11.4 Hz), 3.74 (dd, 1 H, J = 8.8, 10.6 Hz), 4.21 (d, 2 H, J = 5.9 Hz), 5.50 (dt, 1 H, J = 1.1, 5.9 Hz); ^{13}C NMR (75 MHz in $CDCl_3$) δ = –5.2, 18.3, 25.9, 28.6, 31.9, 50.3, 53.7, 59.5, 59.8, 74.4, 74.5, 131.6, 131.7; MS *m/z* 328 (M^+, 0.2%), 253 (10), 235 (11), 223 (10), 105 (57), 93 (27), 91 (33), 75 (100); HRMS *m/z* 328.2069 (328.2070 calcd for $C_{17}H_{32}O_4Si$, M^+).

(3*R*,4*S*,5*S*,6*S*)-4-{(1*E*)-3-Hydroxy-1-methylpropen-1-yl}-5,6-diacetoxy-1-oxaspiro[2.5]octane (47). A solution of compound **46** (20.3 mg, 0.0618 mmol) in acetic anhydride (0.3 ml) and pyridine (0.6 ml) was stirred at room temperature for 9 h. The mixture was concentrated to give crude acetate, which was used for next reaction without purification. To a solution of the crude acetate in THF (0.5 ml) at room temperature was added 1.0 mol dm^{-3} solution of tetra-*n*-butylammonium fluoride in THF (0.124 ml, 0.124 mmol), and the mixture was stirred at room temperature for 1.5 h. The reaction mixture was concentrated to give a residue, which was chromatographed on a column of silica gel (2 g), with EtOAc-hexanes (1:1) as eluent, to afford compound **47** (17.0 mg, 92%) as a colorless syrup: $[\alpha]_D^{21}$ –33.1 (*c* 1.10, $CHCl_3$); IR γ_{max} (neat) 3460, 1750, 1740 cm^{-1}; ^1H NMR (270 MHz) δ = 1.30 (m, 1 H), 1.61 (d , 3 H, J = 1.0 Hz), 1.67 (br, 1 H), 1.81-2.12 (m, 3 H), 1.97 and 2.04 (2s, each 3 H), 2.55 and 2.61 (2d, each 1 H, J = 4.6 Hz), 2.67 (d, 1 H, J = 11.5 Hz), 4.13 (d, 2 H, J = 6.6 Hz), 4.94 (ddd, 1 H, J = 4.6, 9.3, 11.7 Hz), 5.37 (dd, 1 H, J = 9.3, 11.5 Hz), 5.50 (dt, 1 H, J = 1.0, 6.6 Hz); ^{13}C NMR (75 MHz in $CDCl_3$) δ = 15.4, 20.7, 21.0, 26.6, 31.3, 50.2, 52.1, 58.7, 58.9, 72.9, 74.0, 130.4, 132.5, 170.1, 170.5; MS *m/z* 280 (M^+–H_2O, 1%), 267 (8), 207 (39), 196 (15), 178 (31), 165 (31), 160 (25), 147 (100); HRMS *m/z* 280.1308 (280.1311 calcd for $C_{15}H_{20}O_5$, M^+–H_2O).

(3*R*,4*S*,5*S*,6*S*)-4-{(1*E*)-3-Chloro-1-methylprop-1-en-1-yl)-5,6-diacetoxy-1-oxaspiro[2.5]octane (48). A solution of **47** (9.2 mg, 0.030 mmol), collidine (81.6 μl, 0.616 mmol), lithium chloride (6.6 mg, 0.154 mmol), and methanesulfonyl chloride (24 μl, 0.31 mmol) in DMF (1 ml) under Ar was stirred at 0 °C for 30 min. The reaction was diluted with water, and the products were extracted three times with EtOAc. The combined organic layer was successively washed with 1.0 mol dm^{-3} aqueous HCl solution, saturated aqueous $NaHCO_3$ solution, and brine, and then dried. Removal of the solvent gave a residue, which was chromatographed on a column of silica gel (1 g), with EtOAc-hexanes (1:4) as eluent, to afford compound **48** (9.8 mg, 100%) as a colorless syrup: $[\alpha]_D^{16}$ –25.8 (*c* 0.82, $CHCl_3$); IR γ_{max} (neat) 1740 cm^{-1}; ^1H NMR (270 MHz) δ = 1.34 (m, 1 H), 1.68 (d, 3 H, J = 1.5 Hz), 1.81-2.12 (m, 3 H), 1.97 and 2.04 (2s, each 3 H), 2.55 and 2.59 (2d, each 1 H, J = 4.6 Hz), 2.71 (d, 1 H, J = 11.5 Hz), 4.02 (d, 2 H, J = 8.1 Hz), 4.94 (ddd, 1 H, J = 4.5, 9.3, 11.5 Hz), 5.38 (dd, 1 H, J = 9.3, 11.5 Hz), 5.56 (dt, 1 H, J = 1.5, 8.1 Hz); ^{13}C NMR (75 MHz in $CDCl_3$) δ = 14.7, 20.7. 21.0, 26.6, 31.4, 39.8, 50.2, 52.3, 58.8, 72.4, 73.9, 126.8, 136.8, 169.9, 170.5; MS *m/z* 318 ($M(^{37}Cl)^+$, 0.4%), 316 (M^+, 1.2%), 281 (11), 267 (11), 221 (31), 214 (49), 207 (57), 196 (35), 161 (100); HRMS *m/z* 316.1075 (316.1077 calcd for $C_{15}H_{21}O_5Cl$, M^+).

(3*R*,4*S*,5*S*,6*S*)-4-{(1*E*)-1,5-Dimethylhexa-1,4-dien-1-yl}-5,6-diacetoxy-1-oxaspiro[2.5]octane (49). A solution of **48** (12.8 mg, 0.0384 mmol), tetrakis(triphenylphosphine)-palladium(0) (4.2 mg, 3.8 μmol), and tributylisobutenyltin (**31**) (26.6 mg, 0.077 mmol) in THF (1.5 ml) in a sealed tube was stirred under Ar at 40 °C for 5 days. The reaction mixture was concentrated to give a residue, which was chromatographed on a column of silica gel (5 g), with EtOAc-hexanes (1:10) as eluent, to afford compound **49** (9.8 mg, 72%) as a colorless syrup: $[\alpha]_D^{23}$ –20.6 (*c* 0.40, $CHCl_3$); IR γ_{max} (neat) 1750 cm^{-1}; ^1H NMR (270 MHz) δ = 1.30 (m, 1 H), 1.55 (d, 3 H, J = 1.2 Hz), 1.60 (d, 3 H, J = 1.5 Hz), 1.67 (d, 3 H, J = 1.5 Hz), 1.82-2.11 (m, 3 H), 1.94 and 2.04 (2s, each 3 H), 2.52 and 2.61 (2d, each 1 H, J = 4.9 Hz), 2.62 (d, 1 H, J = 11.5 Hz), 2.64 (m, 2 H), 4.93 (ddd, 1 H, J = 4.5, 9.5, 11.7 Hz), 5.01 (ddt, 1 H, J = 1.5, 1.5,

7.1 Hz), 5.22 (dt, 1 H, J = 1.2, 7.1 Hz), 5.34 (dd, J = 9.5, 11.5 Hz, 1 H); ^{13}C NMR (75 MHz in $CDCl_3$) δ = 14.4, 17.7, 20.7, 21.1, 25.6, 26.7, 26.9, 31.4, 50.4, 52.7, 59.2, 72.7, 74.2, 122.2, 129.0, 130.6, 131.9, 169.8, 170.6; MS *m/z* 336 (M^+, 1%), 276 (4), 267 (5), 234 (8), 216 (17), 207 (34), 187 (100); HRMS *m/z* 336.1939 (336.1937 calcd for $C_{19}H_{28}O_5$, M^+).

(3*R*,4*S*,5*S*,6*S*)-4-{(1*E*)-1,5-Dimethylhexa-1,4-dien-1-yl}-1-oxaspiro[2.5]octane-5,6-diol (50). To a solution of compound **49** (6.9 mg, 0.0205 mmol) in MeOH (1 ml) at room temperature was added 1.0 mol dm^{-3} solution of NaOMe in MeOH (123 μl, 0.123 mmol), and the mixture was stirred at room temperature for 25 min. The reaction was quenched with a buffer solution (pH = 7, prepared from 0.2 mol dm^{-3} aqueous NaH_2PO_4 solution and 0.2 mol dm^{-3} aqueous NaOH solution), and the products were extracted with EtOAc (x4). The combined organic layer was washed with brine and dried, and then concentrated to give a residue, which was chromatographed on a column of silica gel (1 g), with EtOAc-hexanes (1:1) as eluent, to afford compound **50** (5.9 mg, 99%) as a colorless syrup: $[\alpha]_D^{22}$ –60.5 (*c* 0.30, $CHCl_3$); IR γ_{max} (neat) 3390 cm^{-1}; ^{1}H NMR (270 MHz) δ = 1.29 (m, 1 H), 1.62 (d, 3 H, J = 1.2 Hz), 1.65 (d, 3 H, J = 1.5 HZ), 1.69 (d, 3 H, J = 1.5 Hz), 1.75 (m, 1 H), 1.93-2.36 (m, 3 H), 2.38 (d, 1 H, J = 11.0 Hz), 2.49 (d, 1 H, J = 4.9 Hz), 2.51 (bd, 1 H, J = 2.4 Hz), 2.56 (d, 1 H, J = 4.9 Hz), 2.73 (bdd, 2 H, J = 7.3, 8.5 Hz), 3.60 (m, 1 H), 3.73 (ddd, 1 H, J = 2.4, 8.5, 11.0 Hz), 5.07 (ddt, 1 H, J = 1.5, 1.5, 8.5 Hz), 5.30 (dt, 1 H, J = 1.2, 7.3 Hz, 1 H); ^{13}C NMR (75 MHz in $CDCl_3$) δ = 17.7, 25.6, 27.0, 28.6, 31.9, 50.4, 54.1, 59.5, 74.5, 74.6, 122.2, 129.6, 131.1, 132.2; MS *m/z* 252 (M^+, 1%), 234 (2), 183 (62), 165 (50), 147 (32), 123 (26), 119 (37), 109 (100); HRMS *m/z* 252.1723 (252.1725 calcd for $C_{15}H_{24}O_3$, M^+).

FR65814 (1). To a solution of **50** (5.9 mg, 0.0233 mmol) in CH_2Cl_2 (1 ml) under Ar at –18 °C were added vanadyl acetylacetonate (0.3 mg, 1.2 μmol) and 5.0-6.0 mol dm^{-3} solution of *tert*-butyl hydroperoxide in decane (0.014 ml, 0.070-0.084 mmol), and the resulting mixture was stirred at –18 °C for 18 h. To the reaction mixture was added dimethyl sulfide (0.1 ml), and the mixture was further stirred at 0 °C for 30 min. The reaction mixture was concentrated to give a residue, which was chromatographed on a column of silica gel (1 g), with EtOAc-hexanes (1:1) as eluent, to afford first, 2',3'-diepi-FR65814 (**51**) (0.6 mg, 9%) as a colorless syrup: IR γ_{max} (neat) 3420 cm^{-1}; ^{1}H NMR (270 MHz) δ = 1.21 (m, 1 H), 1.34 (s, 3 H), 1.50-2.08 (m, 5 H), 1.65 and 1.74 (2d, each 3 H, J = 1.5 Hz), 2.14 (ddd, 1 H, J = 7.1, 7.4, 14.9 Hz), 2.32 (ddd, 1 H, J = 5.9, 7.4, 14.9 Hz), 2.62 (d, 1 H, J = 4.1 Hz), 2.92 (bm, 1 H), 3.13 (bm, 1 H), 3.53 (ddd, 1 H, J = 4.4, 8.5, 11.0 Hz), 3.44 (m, 1 H), 3.58 (m, 1 H), 5.19 (dddd, 1 H, J = 1.5, 1.5, 7.4, 7.4 Hz); MS *m/z* 268 (M^+, 0.8%), 181 (13), 169 (21), 109 (96), 95 (100); HRMS *m/z* 268.1685 (268.1674 calcd for $C_{15}H_{24}O_4$, M^+). Further elution gave FR65814 (**1**) (4.4 mg, 70%) as needles: M.p. 39-40 °C (from Et_2O-hexanes); $[\alpha]_D^{22}$ –41.6 (*c* 0.25, MeOH); {natural FR 65814: M.p. 39-40 °C,[24] mixed M.p. 39-40 °C[24]; $[\alpha]_D^{23}$ –38.4 (*c* 2.4, MeOH)[1]}; IR γ_{max} (neat) 3400 cm^{-1}; ^{1}H NMR (270 MHz) δ = 1.21 (m, 1 H), 1.30 (s, 3 H), 1.41 (d, 1 H, J = 11.2 Hz), 1.66 (d, 3 H, J = 1.5 Hz), 1.70 (m, 1 H), 1.76 (d, 3 H, J = 1.5 Hz), 1.94 (m, 1 H), 1.99 (m, 1 H), 2.14 (ddd, 1 H, J = 7.1, 7.4, 14.9 Hz), 2.42 (ddd, 1 H, J = 5.9, 7.4, 14.9 Hz), 2.55 (d, 1 H, J = 4.3 Hz), 2.61 (dd, 1 H, J = 5.9, 7.1 Hz), 2.73 (br, 1 H), 2.77 (bd, 1 H, J = 3.7 Hz), 2.84 (d, 1 H, J = 4.3 Hz), 3.53 (ddd, 1 H, J = 4.4, 8.5, 11.0 Hz), 3.88 (ddd, 1 H, J = 3.7, 8.5, 11.2 Hz), 5.17 (dddd, 1 H, J = 1.5, 1.5, 7.4, 7.4 Hz); ^{13}C NMR (75 MHz in $CDCl_3$) δ = 13.7, 18.1, 25.8, 27.2, 28.0, 32.3, 49.3, 52.2, 58.5, 59.6, 61.8, 75.0, 75.2, 117.8, 135.5. The spectral data were fully identical with those of natural FR 65814. MS *m/z* 268 (M^+, 0.3%), 181 (9), 169 (11), 149 (20), 109 (36), 95 (51), 86 (72), 84 (100), 55 (41); HRMS *m/z* 268.1672 (268.1674 calcd for $C_{15}H_{24}O_4$, M^+).

REFERENCES AND NOTES

1. Hatanaka, H.; Kino, T.; Hashimoto, M.; Tsurumi, Y.; Kuroda, A.; Tanaka, H.; Goto, T.; Okuhara, M. *J. Antibiot.* **1988**, *41*, 999.
2. DiPaolo, J. A.; Tarbell, D. S.; Moore, G. E. in *Antibiotics Annual 1958-1959*, ed. Welch, H.; Marti-Ibanez, F. Medical Encyclopedia, Inc., New York, 1959, p. 451.
3. (a) Ingber, D. E.; Fujita, T.; Kishimoto, S.; Sudo, K.; Kanematsu, T.; Brem, H.; Folkman, J. *Nature* **1990**, *348*, 555; Ingber, D. E.; *Semin. Cancer Biol.* **1992**, *3*, 57; Folkman, J.; Ingber, D. E. *Semin. Cancer Biol.* **1992**, *3*, 89; (b) Sin, N.; Meng, L.; Wang, M. Q. W.; Wen, J. J.; Bornmann, W. G.; Crews, C. M. *Proc. Natl. Acad. Sci. USA* **1997**, *94*, 6099; Griffith, E. C.; Su, Z.; Turk, B. E.; Chen, S.; Chang, Y.-H.; Wu, Z.; Biemann, K.; Liu, J. O. *Chem. Biol.* **1997**, *4*, 461.

4. Hayashi, M.; Kim, Y.-P.; Takamatsu, S.; Preeparme, S.; Komiya, T.; Masuda, R.; Tanaka, H.; Komiyama, K.; Omura, S. *J. Antibiot.* **1996**, *49*, 641; Takamatsu, S.; Kim, T.-P.; Komiya, T.; Sunazuka, T.; Hayashi, M.; Tanaka, H.; Komiyama, K.; Omura, S. *J. Antibiot.* **1996**, *49*, 635.
5. (a) Corey, E. J.; Snider, B. B. *J. Am. Chem. Soc.* **1972**, *94*, 2549; (b) Kim, D.; Ahn, S. K.; Bae, H.; Choi, W. J.; Kim, H. S. *Tetrahedron Lett.* **1997**, *38*, 4437; (c) Corey, E. J.; Dittami, J. P. *J. Am. Chem. Soc.* **1985**, *107*, 256; (d) Bath, S.; Billington, D. C.; Gero, S. D.; Quiclet-Sire, B.; Samadi, M. *J. Chem. Soc., Chem. Commun.* **1994**, 1495; Corey, E. J.; Guzman-Perez, A.; Noe, M. C. *J. Am. Chem. Soc.* **1994**, *116*, 12109; Barco, A.; Benetti, S.; De Risi, C.; Marchetti, P.; Pollini, G.; Zanirato, V. *Tetrahedron: Asymmetry* **1998**, *9*, 2857.
6. (a) Ferrier, R. J. *J. Chem. Soc., Perkin Trans. 1* **1979**, 1455; Ferrier, R. J.; Hains, S. R. *J. Chem. Soc., Perkin Trans. 1* **1985**, 2413. For a review, see (b) Ferrier, R. J.; Middleton, S. *Chem. Rev.* **1993**, *93*, 2779.
7. Utilization of Ferrier's carbocyclization in natural product synthesis: see Barton, D. H. R.; Augy-Dorey, S.; Camara, J.; Dalko, P.; Delaumeny, J. M.; Gero, S. D.; Quiclet-Sire, B.; Stütz, P. *Tetrahedron* **1990**, *46*, 215; Ferrier, R. J.; Stütz, A. E. *Carbohydr. Res.* **1990**, *200*, 237; Miyamoto, M.; Baker M. L.; Lewis, M. D. *Tetrahedron Lett.* **1992**, *33*, 3725; Sakairi, N.; Hayashida, M.; Amano, A.; Kuzuhara, H. *J. Chem. Soc., Perkin Trans. 1* **1990**, 1301; Takahashi, S.; Terayama, H.; Kuzuhara, H. *Tetrahedron Lett.* **1991**, *32*, 5123; Sato, K.; Sakuma, S.; Muramatsu, S.; Bokura, M. *Chem. Lett.* **1991**, 1473; Estevez, V. A.; Prestwich, G. D. *J. Am. Chem. Soc.* **1991**, *113*, 9885; Bender, S. L.; Budhu, R. J. *J. Am. Chem. Soc.* **1991**, *113*, 9883; Dyong, I.; Hagedorn, H.-W.; Thiem, J. *Liebigs Ann. Chem.* **1986**, 551; Fisher, M. J.; Myers, C. D.; Joglar, J.; Chen, S.-H.; Danishefsky, S. J. *J. Org. Chem.* **1991**, *56*, 5826; Chrétien, F.; Ahmed, S. I.; Masion, A.; Chapleur, Y. *Tetrahedron* **1993**, *49*, 7463; Ermolenko, M. S.; Olesker, A.; Lukacs, G. *Tetrahedron Lett.* **1994**, *35*, 715; Ermolenko, M. S.; Lukacs, G.; Poiter, P. *Tetrahedron Lett.* **1995**, *36*, 2465; Park, T. K.; Danishefsky, S. J. *Tetrahedron Lett.* **1995**, *36*, 195; Chida, N.; Ohtsuka, M.; Nakazawa, K.; Ogawa, S. *J. Org. Chem.* **1991**, *56*, 2976; Chida, N.; Ohtsuka, M.; Ogawa, S. *J. Org. Chem.* **1993**, *58*, 4441; Chida, N.; Jitsuoka, M.; Yamamoto, Y.; Ohtsuka, M.; Ogawa, S. *Heterocycles* **1996**, *43*, 1385; Chida, N.; Sugihara, K.; Amano, S.; Ogawa, S. *J. Chem. Soc., Perkin Trans. 1* **1997**, 275; Takahashi, S.; Iimori, T.; Ikegami, S. *Tetrahedron Lett.* **1998**, *39*, 6939.
8. Preliminary communication: Amano, S.; Ogawa, N.; Ohtsuka, M.; Ogawa, S.; Chida, N. *Chem. Commun.* **1998**, 1263.
9. Catalytic version of Ferrier's carbocyclization with Hg salts, see (a) Chida, N.; Ohtsuka, M.; Ogura, K., Ogawa, S. *Bull. Chem. Soc. Jpn.* **1991**, *64*, 2118. (b) Machado, A. S.; Olesker, A.; Lukacs, G. *Carbohydr. Res.* **1985**, *135*, 231; Machado, A. S.; Olesker. S.; Castillon, S.; Lukacs, G. *J. Chem. Soc., Chem. Commun.* **1985**, 330: with Pd salts, see (c) Adam, S. *Tetrahedron Lett.* **1988**, *29*, 6589; (d) Iimori, T.; Takahashi, H.; Ikegami, S. *Tetrahedron Lett.* **1996**, *37*, 649.
10. Gemal, A. L.; Luche, J.-L. *J. Am. Chem. Soc.* **1981**, *103*, 5454.
11. Barton, D. H. R.; McCombie, S. W. *J. Chem. Soc., Parkin Trans. 1* **1975**, 1574.
12. Miyashita, M.; Yoshikoshi, A.; Grieco, P. A. *J. Org. Chem.* **1977**, *42*, 3772.
13. Johnson, W. S.; Werthemann, L.; Bartlett, W. R.; Brockson, T. J.; Li, T.-T.; Faulker, D. J.; Petersen, M. R. *J. Am. Chem. Soc.* **1970**, *92*, 741.
14. Chang, F. C.; Wood, N. F. *Tetrahedron Lett.* **1964**, 2969.
15. Ley, S. V.; Norman, J.; Griffith, W. P.; Marsden, S. P. *Synthesis* **1994**, 639.
16. Ito, Y.; Hirao, T.; Saegusa, T. *J. Org. Chem.* **1978**, *43*, 1011.
17. Sheffy, F. K.; Godschalx, J. P.; Stille, J. K. *J. Am. Chem. Soc.* **1984**, *106*, 4833; Stille, J. K. *Angew. Chem. Int. Ed. Engl.* **1986**, *25*, 508.
18. Saihi, M. L.; Pereyre, M. *Bull. Soc. Chim. Fr.* **1977**, 1251.
19. Sharpless, K. B.; Michaelson, R. C. *J. Am. Chem. Soc.* **1973**, *95*, 6136.
20. Birth, A. J.; Subba Rao, G. S. R. *Tetrahedron Lett.* **1968**, 3797.
21. Corey, E. J.; Chaykovsky, M. *J. Am. Chem. Soc.* **1965**, *87*, 1353.
22. Krief, A. *Tetrahedron* **1980**, *36*, 2531.
23. Miehlich, E. D.; Daniels, K.; Eickhoff, D. J. *J. Am. Chem. Soc.* **1981**, *103*, 7690.
24. These data of natural FR65814 were measured in our laboratory on material kindly supplied by Fujisawa Pharmceutical Co., Ltd.