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Enantioselective Total Synthesis of (+)-Stoechospermol *Via* Stereoselective Intramolecular (2+2) Photocycloaddition of the Chiral Butenolide[1]

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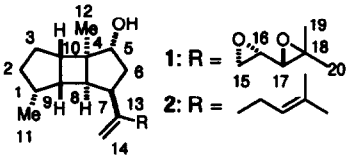
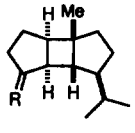
Abstract: Enantioselective total synthesis of (+)-stoechospermol **2**, a representative of spatane diterpenes having a *cis,anti,cis*-tricyclo[5.3.0.0^{2,6}]decane skeleton, was achieved by employing a stereo- and regioselective intramolecular (2+2) photocycloaddition of (*S*)-γ-hydroxymethyl-γ-butenolide-derived ester **10**.

A (2+2) photocycloaddition is a versatile methodology for constructing four membered-carbo- and heterocycles.[2] An asymmetric photocycloaddition is one of the recent challenge in synthetic organic chemistry.[3] Previously we have reported an asymmetric total synthesis of bourbonene sesquiterpenes **3** and **4** using an intermolecular asymmetric (2+2) photocycloaddition of a chiral butenolide with a cyclopentene derivative.[4] In the present article we describe a full detail of highly stereoselective intramolecular (2+2) photocycloaddition and application to an enantioselective total synthesis of stoechospermol **2**, a representative of spatane diterpenes.[5,6,7]





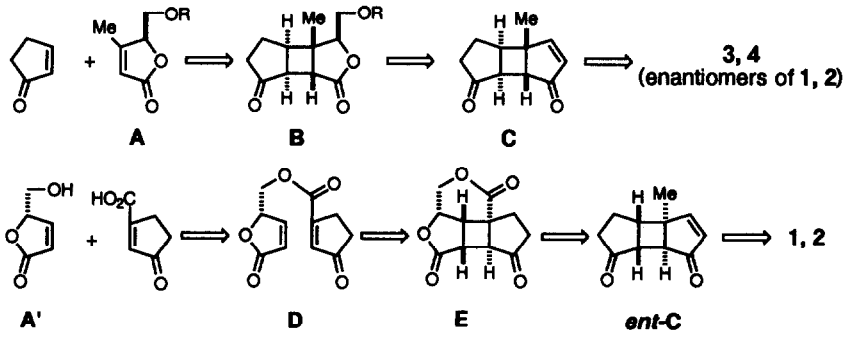
3: R = O

4: R = CH_2

Spatane diterpenes such as spatol **1** and stoechospermol **2** have been isolated from marine brown algae and known as natural products of unique structure characterized by a *cis,anti,cis*-tricyclo[5.3.0.0^{2,6}]decane ring system. In addition, **1** is known to be endowed with remarkable biological properties including a potent inhibition of cell replication.[6] It is interesting in that spatane diterpenes, **1** and **2**, have the same carbocyclic skeleton as bourbonene sesquiterpenes such as **3** and **4**,[8] however, antipodal each other with regard to tricyclic carbon skeleton except for the configuration at the carbon attaching side chain.

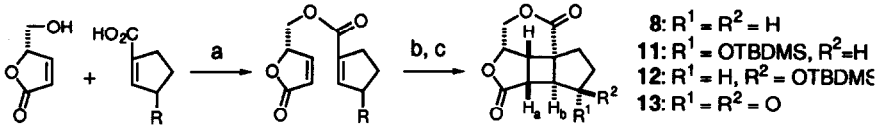
As part of our project to engage in the enantioselective total synthesis of both spatane and bourbonene terpenes in optically pure forms, we designed asymmetric intermolecular (2+2) photocycloaddition of a chiral butenolide **A** with cyclopentene derivative.[9] In that methodology, the least hindered approach of cyclopentene derivative to **A** created the chiral centers of **B** and **C**, and resulted in the successful total synthesis of optically pure **3** and **4**.[4]

The synthesis of spatane diterpenes of antipodal tricyclic carbon skeleton with bourbonene sesquiterpene required the reverse sense of stereoselectivity in the (2+2) photocycloaddition of the chiral butenolide. The method designed for this purpose is the intramolecular (2+2) photocycloaddition of **D**, prepared from **A'** and cyclopentenecarboxylic acid derivative. Because of highly stereo- and regioselective nature, the intramolecular cycloaddition has been applied into the natural products synthesis.[10] In our particular case, molecular models of transition states and cycloadducts indicate that the ester linkage between **A'** and cyclopentene parts is expected to control regio- and stereochemistry of the cycloaddition, allowing the cyclopentene part to approach from the sterically more hindered face of the butenolide to afford **E**. Then, subsequent manipulations will convert **E** into ***ent*-C** that possesses the antipodal configuration with **C**.

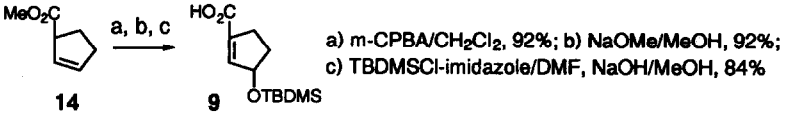


Stereochemistry of Intramolecular Photocycloaddition

The intramolecular (2+2) photocycloaddition reaction began with a model study using **7**. The simple ester **7** was prepared by esterification of butenolide **5**[11,12] with **6**.[13] On irradiation of **7** in acetonitrile using a low pressure mercury lamp at 15 °C, the cycloaddition afforded a single product **8** in 78% yield. The product was isolated by column chromatography, and the structure was assigned based on the proton nuclear magnetic resonance (NMR) and infra red (IR) spectra. The *cis,anti,cis*-arrangement of **8** was ascertained by the coupling constant of the carbonyl α-proton (H_a) with H_b. For the adduct **8**, signal of H_a



a) DCC-DMAP/CH_2Cl_2, 82% for **7**, 96% for **10**; b) hν/CH_3CN, 78% for **8**; 36% for **11**, 25% for **12**; c) CrO_3-H_2SO_4/HF-acetone-H_2O, 69% from **11** to **13**, 49% from **12** to **13**



a) m-CPBA/CH_2Cl_2, 92%; b) NaOMe/MeOH, 92%; c) TBDMSCl-imidazole/DMF, NaOH/MeOH, 84%

appeared at 2.67 ppm and its coupling constant with H_b is 3 Hz, which corresponds to the *trans* relationship. Furthermore, the existence of saturated δ-lactone is evidenced by the IR in which the corresponding carbonyl absorption appeared at 1725 cm^{-1}.

Having established the stereo- and regiochemistry in the intramolecular (2+2) photocycloaddition of the simple ester **7**, we turned our attention to the synthesis of spatane diterpene.

Intramolecular Photocycloaddition of 10

The ester **10**, a diastereomeric mixture due to the racemic cyclopentene part, was prepared by esterification of optically pure (-)-**5** with the corresponding racemic **9** which was prepared from methyl cyclopent-2-ene-1-carboxylate[14] in four steps.[15] The irradiation of **10** under the same conditions for **7** afforded the two products **11** and **12** in 36 and 25% isolated yield, respectively. The stereochemistry of each adduct was determined based on the NMR. For the adduct **11**, the signal corresponding to H_b appeared at 2.81 ppm and its coupling constant with an adjacent proton attaching at the silyloxy bearing carbon was 0 Hz, indicating that the corresponding dihedral angle is about 90 deg. On the other hand, the adduct **12** showed the corresponding signal at 3.26 ppm with coupling constant of 7 Hz, indicating the dihedral angle of about 30 deg. Structures of **11** and **12** obtained by the Cache force field agree well the present assignment.

By the oxidation of silyloxyl group to ketone, both **11** and **12** were converted to the same ketone **13**, demonstrating that these two adducts differ only by the configuration of the carbon bearing silyloxyl group, and, hence, the steric course of the cycloaddition was governed only by the chiral center in the butenolide part not by one in cyclopentene part.

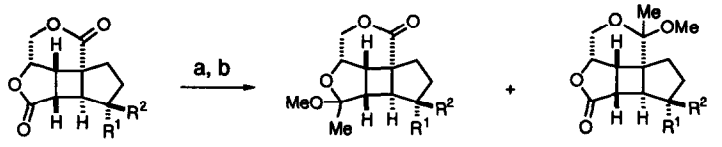
Since the configurations of the four membered rings of both cycloadducts **11**, **12** were confirmed, further transformation of the cycloadducts to the intermediate of the type ***ent*-C** was the next task.

Differentiation of Two Lactone Carbonyl Groups Affected by Remote α-Alkoxy Group

The transformation of **E** to ***ent*-C** requires independent manipulations of the two lactone carbonyl groups, reduction the δ-lactone carbonyl to methyl group, and C-C bond formation at the γ-lactone carbonyl to methyl ketone. In the original design, the differentiation of these two carbonyl groups relies on the steric environment, the δ-lactone carbonyl suffering much hindrance by the quaternary α carbon-center than the γ-lactone carbonyl.

Upon treatment of **11** with methyllithium followed by acetal formation, two products **15** and **16** were obtained in 59 and 26% yield, respectively, and the major product was fortunately the desired **15**.

However, the same treatment of **12** afforded **18** as a major product in 52% yield and **17** in only 7% yield, by the preferential reaction at the undesired δ-lactone part.



11: R^1 = OTBDMS, R^2 = H **15**: R^1 = OTBDMS, R^2 = H **16**: R^1 = OTBDMS, R^2 = H
12: R^1 = H, R^2 = OTBDMS **17**: R^1 = H, R^2 = OTBDMS **18**: R^1 = H, R^2 = OTBDMS

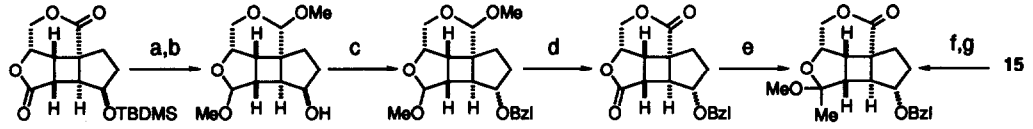
a) MeLi/THF; b) $HC(OMe)_3$-PPTS/CH_2Cl_2, from **11**: 59% for **15**, 26% for **16**; from **12**: 7% for **17**, 52% for **18**

We assumed that the unexpected selectivity observed for **12** could be ascribed to the absence of the blocking alkoxy group near the δ-lactone carbonyl group. Then we determined to invert the alkoxy configuration from β to α and place the alkoxy group near the δ-lactone carbonyl, in advance to the reaction with methyllithium.

The lactone **12** was reduce with DIBAH and subsequently acetalized. The silyl group was then deprotected with hydrogen fluoride affording **19** which was converted into α-benzyl ether **21** by the Mitsunobu inversion[16] and following benzylation and oxidation.

To our delightful and surprise, the reaction of **21** with methyllithium afforded a single product **22** in high selectivity by the preferential reaction at the desired γ-lactone part.

The compound **15** was also converted to **22**, the key intermediate in our synthesis.

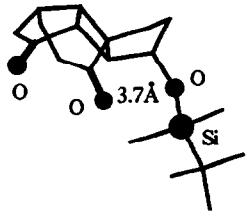


a) DIBAH/THF, $HC(OMe)_3$-TsOH/CH_2Cl_2, 62%; b) aq. HF/MeOH, 91%; c) $PhCO_2H$-DEAD-PPh_3/THF, NaOH/aq. MeOH, 96%, BzlBr-NaH/DMF, 87%; d) AcOH/aq. THF, CrO_3-H_2SO_4/aq. acetone, 99%; e) MeLi/THF, $HC(OMe)_3$-PPTS/CH_2Cl_2, quant; f) aq. HF/MeOH, 74%; g) BzlBr-NaH/DMF, 77%

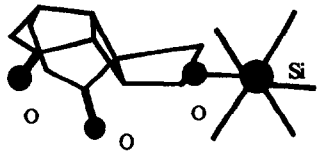
Origin of Chemoselectivity in 11 and 21 vs 12

It is quite interesting in that remote α- and β-alkoxy groups direct the preferential reaction at the γ- and δ-lactone carbonyls, respectively. It is apparent from molecular mechanics (MM) structures calculated by Cache that α- and β-alkoxy groups do not cover any faces of the carbonyls. As shown by the MM structures, differences are the distance between the δ-lactone carbonyl- and ether-oxygens, 3.7Å in **11** and **21** and over 4.4Å in **12**, and the orientation of the lone pairs of ether oxygen, directing to δ-lactone carbonyl oxygen in **11** and **21**.

It is reasonable to assume that lone pairs of ether oxygen would reduce the polarizability and, hence, reactivity of the δ-lactone carbonyl group of **11** and **21**, due to the negative charge around carbonyl oxygen. Indeed this hypothesis was confirmed by molecular orbital calculations (PM3, precise mode in Cache system) of the corresponding alcohol structure. LUMO coefficients of the γ-lactone carbonyl are much greater than those of the δ-lactone in **11** and **21**, on the other hand, in **12** the situation is reversed.



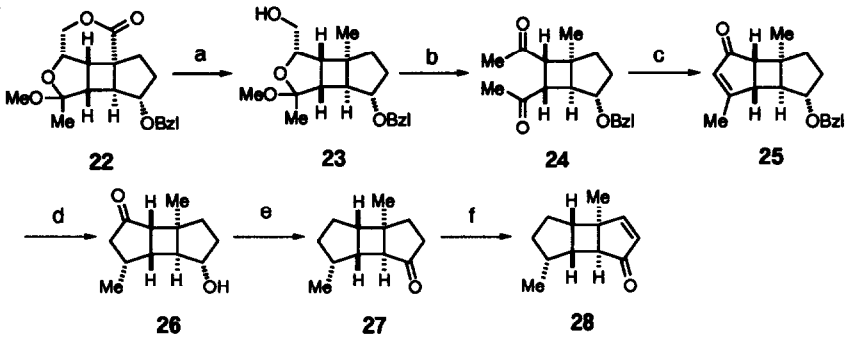
MM structure of 11 (21)



MM structure of 12

Construction of Tricyclo[5.3.0.$0^{2,6}$]decane

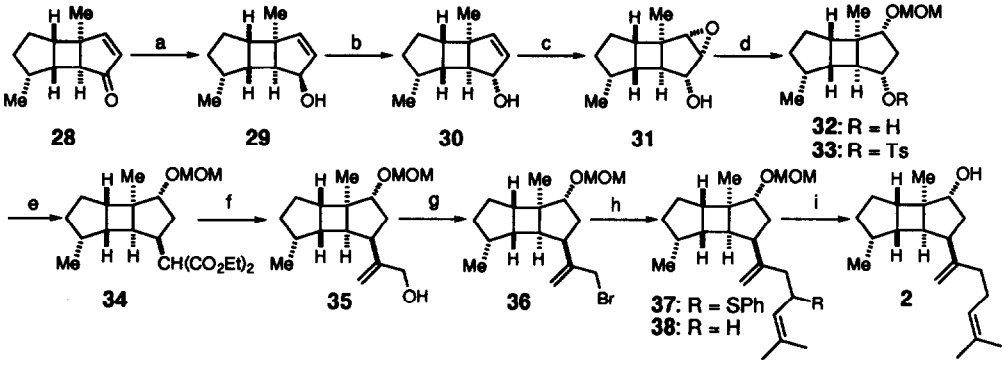
With the differentiation of two carbonyl groups achieved, the δ-lactone in **22** was reduced to angular methyl group of **23** in two steps. Then, construction of the tircyclodecane ring was achieved by aldol condensation[4] of diketone **24**, obtained from **23** in five steps, to give stereo- and regioselectively **25** as a single product. Hydrogenation of the double bond of **25** from the convex face created the C(1) chiral center in the desired sense, and deoxygenation of carbonyl group of **26** and subsequent oxidation of cyclopentanol part into cyclopentenone afforded optically pure tricyclo[5.3.0.$0^{2,6}$]decane **28**, the key intermediate for the synthesis of spatane diterpenes.



a) DIBAH/toluene, quant; NH_2NH_2·H_2O-KOH/diethylene glycol, 53%; b) H_2SO_4/aq. THF, $NaBH_4$/MeOH, $NaIO_4$/aq. AcOEt, MeLi/ether, CrO_3-H_2SO_4/aq. acetone, 67%; c) KOBu-t/t-BuOH, 85%; d) H_2-10%Pd-C/ether, quant; e) NH_2NH_2·H_2O/triethylene glycol, 54%; CrO_3-H_2SO_4/aq. acetone, quant; f) PhSeCl/AcOEt, $NaIO_4$/aq. MeOH, 42%.

Total Synthesis of (+)-Stoechospermol 2

Having accomplished the construction of the desired optically pure key intermediate **28**, the remaining was conversion to **2**. Reduction of **28** with DIBAH gave stereoselectively **29** as a single product by the attack of hydride from the less hindered face. For the introduction of the C(5) hydroxyl group in correct configuration, **30**, obtained by the Mitsunobu inversion of **29** and following hydrolysis, was stereoselectively oxidized into epoxide **31**. Regioselective cleavage of oxirane ring by lithium aluminum hydride and protection of the resultant hydroxyl group afforded **32**. Tosylation of **32** followed by substitution with sodio diethyl malonate proceeded with inversion of the C(7) configuration affording **34**,



a) DIBAH/ether, quant; b) $PhCO_2H$-DEAD-PPh_3/THF, NaOH/aq. MeOH, 71%; c) MCPBA/CH_2Cl_2, 81%; d) 2-methoxypropene-PPTS, $LiAlH_4$/ether, MOMCl-(i-Pr)$_2$NEt/CH_2Cl_2, HCl, 83%; e) TsCl/Py, $NaCH(CO_2Et)_2$/DME, 60%; f) LDA-Vitride/DME, 88%; g) MsCl/2,6-lutidine, LiBr/DMF, 90%; h) n-BuLi-phenyl prenyl sulfide/THF, Li-$EtNH_2$/ether, 33%; i) HCl/aq. MeOH, 71%

in which the configuration at the C(7) was properly established. Reduction of the malonic ester moiety as its enolate afforded allylic alcohol **35**,[17] which was then converted into bromide **36**. By reaction with lithiated phenyl prenyl sulfide and following desulfurization,[18] **36** was converted into **38**. Finally, deprotection of **38** completed the total synthesis to provide **2** as crystalline solid. NMR, IR, and MS spectra of synthetic (+)-**2** were in good agreement with those reported for natural (+)-**2** isolated from marine brown algae.

Conclusion

By employing highly regio- and stereoselective intramolecular (2+2) photocycloaddition as a key step, optically pure tricyclo[5.3.0.0^{2,6}]decane ring was constructed from optically pure butenolide, and this was successfully applied to the first total synthesis of optically pure natural stoechospermol. Combined with previously reported intermolecular (2+2) photocycloaddition,[4] intramolecular version made it possible to access the optically pure tricyclo[5.3.0.0^{2,6}]decanes in both enantiomers from the single chiral butenolide as has been demonstrated in the present total synthesis of optically pure stoechospermol.

Experimental[19]

(-)-(*R*)-4-Hydroxymethylbut-2-en-4-olide 5 A solution of (-)-(*R*)-4-trityloxymethylbut-2-en-4-olide[11] (3.0 g) and 12N HCl (3 mL) in MeOH (300 mL) was stirred at rt for 2 h. Concentration and purification by column chromatography (ether) afforded **5** (0.83 g, 90%) as pale brown solid which was used in the next step without further purification. $[\alpha]_D^{20}$ -125 °(c 0.95, $CHCl_3$). IR ($CHCl_3$) : 3600-3300, 1785, 1760 cm^{-1}. NMR δ: 2.99 (1H, s, OH), 3.77 (1H, dd, J=13, 5 Hz, OC$\underline{H}_2$CHO), 3.99 (1H, dd, J=13, 4 Hz, OC$\underline{H}_2$CHO), 5.16 (1H, br, $OCH_2C\underline{H}O$), 6.17 (1H, dd, J=6, 2 Hz, CH=C$\underline{H}$O), 7.49 (1H, d, J=6 Hz, C$\underline{H}$=CHO).

Confirmation of optical purity of (-)-5 A solution of (-)-**5** (119 mg) in EtOH was hydrogenated over 5% Pd-C (20 mg) under H_2 at rt for 4 h. Filtration, concentration, and purification by column chromatography (ether) gave (+)-4-hydroxybutanolide (116 mg, 96%) as a colorless oil. $[\alpha]_D^{26}$ +31.9 °(c 3.24, EtOH) ($[\alpha]_D^{26}$ +31.3 °(c 2.92, EtOH)).[12] The spectroscopic data were identical with those of the reported.[12]

(-)-(*R*)-4-(Cyclopent-1-ene-1-carbonyloxymethyl)but-2-en-4-olide 7 Dicyclohexylcarbodiimide (DCC) (433 mg, 2.1 mmol) was added to a stirred solution of (-)-**5** (191 mg, 1.68 mmol), **6** (200 mg, 1.79 mmol), and 4-dimethylaminopyridine (DMAP) (15 mg) in dichloromethane (CH_2Cl_2) (3 mL) at 0 °C. The whole was stirred at rt for 2 h, and acetic acid (AcOH) (0.2 mL) was added. After the precipitate was filtered off, the filtrate was washed successively with 10% HCl, and satd. $NaHCO_3$, then dried. Concentration and column chromatography (AcOEt-hexane 1:2) afforded **7** (285 mg, 82%) as a colorless oil. $[\alpha]_D^{20}$ -113 °(c 1.00, $CHCl_3$). IR (neat): 1750, 1710, 1625, 1600 cm^{-1}. NMR δ: 1.92 (2H, quintet, J=8 Hz, $CH_2C\underline{H}_2CH_2$), 2.50 (4H, t, J=8 Hz, $C\underline{H}_2CH_2C\underline{H}_2$), 4.40 (1H, dd, J=5, 12 Hz, OC$\underline{H}_2$CHOCO), 4.47 (1H, dd, J=4, 12 Hz, OC$\underline{H}_2$CHOCO), 5.2-5.4 (1H, m, C$\underline{H}$OCO), 6.15 (1H, dd, J=2, 6 Hz, OCC$\underline{H}$=CH), 6.74 (1H, s, C$\underline{H}$=CCO$_2$), 7.57 (1H, dd, J=1, 6 Hz, OCCH=C$\underline{H}$). MS m/z: 98 (M$^+$-$C_6H_8O_2$).

(-)-(1*S*,5*R*,9*S*,10*R*,13*S*)-3,12-Dioxatetracyclo[8.2.1.0.^{5,9}0^{5,13}]tridecan-4,11-dione 8 A solution of **7** (90 mg) in acetonitrile (4.5 mL) was internally irradiated with 10 W low pressure mercury lamp at 15 °C for 3 h. Concentration and column chromatography (AcOEt-benzene 1:2) afforded **8** (70 mg, 78%) as colorless prisms of mp 128-130 °C (AcOEt). $[\alpha]_D^{20}$ -34.0 °(c 0.77, $CHCl_3$). IR (KBr): 1760, 1725 cm^{-1}. NMR δ: 1.7-2.3 (6H, m, $(C\underline{H}_2)_3$), 2.64 (1H, dd, J=3, 7 Hz, C$\underline{H}$CO), 2.94 (1H, t, J=7 Hz, C$\underline{H}$CHOCO), 3.05 (1H, br, $CH_2C\underline{H}CHCO$), 4.39 (1H, dd, J=1, 13 Hz, OC$\underline{H}_2$CH), 4.6-4.9 (2H, m, OC$\underline{H}_2$CH). MS m/z: 208 (M$^+$). Anal. Calcd for $C_{11}H_{12}O_4$: C, 63.45; H, 5.81. Found C, 63.73; H, 5.86.

(±)-3-*tert*-Butyldimethylsilyloxy-1-cyclopentane-1-carboxylic acid 9 A solution of methyl 2-cyclopentene-1-carboxylate (**14**) (13.8 g, 0.11 mole) and 85% *m*-chloroperbenzoic acid (MCPBA) (24 g, 0.12 mole) in CH_2Cl_2 (300 mL) was stirred at rt for 15 h. After concentration, the residue was taken up into ether (200 mL) and washed successively with 10% $Na_2S_2O_3$, satd. $NaHCO_3$, and satd. NaCl, then dried. Concentration gave methyl 2,3-epoxycyclopentane-1-carboxylate (10.4 g, 92%) as a pale yellow oil. IR (neat): 1735 cm^{-1}. NMR δ: 1.5-2.3 (4H, m, $(C\underline{H}_2)_2$), 2.7-3.0 (0.5H, m, C$\underline{H}$CO$_2$CH$_3$), 3.0-3.2 (0.5 H, m, C$\underline{H}$CO$_2$CH$_3$), 3.4-3.7 (2 H, m, C$\underline{H}$(O)C$\underline{H}$), 3.71 (1.5 H, s, OC$\underline{H}_3$), 3.75 (1.5 H, s, OC$\underline{H}_3$). MS m/z: 142 (M$^+$). A solution of above epoxy ester (11.3 g, 80 mmol) and sodium methoxide (8 mmol) in MeOH (4 mL) was stirred at rt for 2.5 h and acidified by 10% HCl. After concentration, the residue was taken up into AcOEt (100 mL), and washed successively with satd. $NaHCO_3$ and satd. NaCl, then dried. Concentration gave methyl 3-hydroxy-1-cyclopentene-1-carboxylate (10.4 g, 92%) as a yellow oil. IR (neat): 3400, 1720, 1630 cm^{-1}. NMR δ: 1.6-2.9 (5H, m, O$\underline{H}$ and $(C\underline{H}_2)_2$), 3.75 (3H, s, OC$\underline{H}_3$), 4.8-5.0 (1H, m, $CH_2C\underline{H}$(OH)C=C), 6.64 (1H, t, J=2 Hz, C$\underline{H}$=CCO$_2$). MS m/z: 142 (M$^+$). A solution of above

hydroxyester (5.7 g, 40 mmol), *tert*-butyldimethylsilyl chloride (7.4 g, 49 mmol), and imidazole (3.4 g, 50 mmol) in DMF (45 mL) was stirred at rt for 2 h and diluted with benzene (500 mL). After successive washing with water and satd. NaCl, the organic layer was dried. Concentration afforded crude silyl ether of the hydroxyester (10.9 g), and this was dissolved in MeOH (50 mL). After addition of 1N NaOH (40 mL, 40 mmol), the whole was stirred at rt for 12 h. After concentration, the residue was acidified with 10% HCl, and then extracted with CH_2Cl_2 (50 mL x 3). The extract was washed with water and dried. Concentration afforded **9** (8.2 g, 84% from hydroxyester) as colorless needles of mp 80-81.5 °C (AcOEt-hexane). IR (KBr): 3600-2400, 1680, 1630 cm^{-1}. NMR δ: 0.10 (6H, s, $(CH_3)_2$), 0.89 (9H, s, $(CH_3)_3$), 1.5-1.9 (1H, m, $(CH_2)_2$), 2.1-2.9 (3H, m, $(CH_2)_2$), 4.8-5.0 (1H, m, CHOSi), 6.5-6.6 (1H, m, $CH{=}CCO_2H$), 7.90-8.40 (1H, br, OH). MS m/z: 242 (M^+). Anal. Calcd for $C_{12}H_{22}O_3Si$: C, 59.46; H, 9.15. Found C, 59.31; H, 9.29.

(-)-(*R*)-4-(3-*tert*-Butyldimethylsilyloxycyclopent-1-ene-1-carbonyloxymethyl)but-2-en-4-olide 10 DCC (4.41 g, 21 mmol) was added to a stirred solution of (-)-**5** (2.44 g, 21 mmol), **9** (5.18 g, 21 mmol), and DMAP (0.31 g) in CH_2Cl_2 (60 mL) at 0 °C. The whole was stirred at 0 °C for 2 h, and AcOH (2 mL) was added. Work up afforded (-)-**10** (6.94 g, 96%) as a colorless oil. $[\alpha]_D^{20}$ -55.8 °(c 1.19, $CHCl_3$). IR (neat): 1780, 1720 cm^{-1}. NMR δ: 0.08 (6H, s, $(CH_3)_2$), 0.90 (9H, s, $(CH_3)_3$), 1.6-2.0 (1H, m, $(CH_2)_2$), 2.1-2.7 (3H, m, $(CH_2)_2$), 4.42 (2H, d, J=4 Hz, OCH_2CHO), 4.8-5.0 (1H, m, OCH_2CHO), 5.2-5.3 (1H, m, CHOSi), 6.19 (1H, dd, J=6, 2 Hz, CH=CH), 6.61 (1H, t, J=2 Hz, CH=C), 7.42 (1H, dd, J=6, 1 Hz, CH=CH).

(-)-(1*S*,5*S*,8*S*,9*S*,10*R*,13*S*)-8-*tert*-Butyldimethylsilyloxy-3,12-dioxatetracyclo-[8.2.1.0.^{5,9}0^{5,13}]tridecan-4,11-dione 11 and (+)-(1*S*,5*S*,8*R*,9*S*,10*R*,13*S*)-8-*tert*-Butyldimethylsilyloxy-3,12-dioxatetracyclo[8.2.1.0.^{5,9}0^{5,13}]tridecan-4,11-dione 12 According to the same procedure for **7**, (-)-**10** (102 mg) was irradiated to give a mixture of **11** and **12** as an oil. Column chromatography (AcOEt-benzene 1:3) afforded (-)-**11** (37 mg, 36%) as colorless plates of mp 203-204 °C (AcOEt-hexane) and (+)-**12** (26 mg, 25%) as colorless needles of mp 154-155.5 °C (AcOEt-hexane). (+)-**11**: $[\alpha]_D^{20}$ -32.6 °(c 1.13, $CHCl_3$). IR (KBr): 1770, 1720 cm^{-1}. NMR δ: 0.08 (6H, s, $(CH_3)_2$), 0.88 (9H, s, $(CH_3)_3$), 1.7-2.2 (4H, m, $(CH_2)_2$), 2.68 (1H, dd, J=3, 7 Hz, CHCO), 2.81 (1H, d, J=3 Hz, CHCHCO), 2.94 (1H, t, J=7 Hz, OCH_2CHCH), 4.2-4.5 (2H, m, SiOCH, OCH_2CHO), 4.7-4.9 (2H, m, OCH_2CHO). MS m/z: 343 (M^+-CH_3). Anal. Calcd for $C_{17}H_{26}O_5Si$: C, 60.32; H, 7.74. Found C, 60.10; H, 7.75. (+)-**12**: $[\alpha]_D^{20}$ +8.85 °(c 1.04, $CHCl_3$). IR (KBr): 1770, 1720 cm^{-1}. NMR δ: 0.08 (6H, s, $(CH_3)_2$), 0.90 (9H, s, $(CH_3)_3$), 1.6-2.6 (4H, m, $(CH_2)_2$), 2.88 (1H, dd, J=3, 7 Hz, CHCO), 3.26 (1H, dd, J=3, 7 Hz, CHCHCO), 3.01 (1H, t, J=7 Hz, OCH_2CHCH), 4.3-4.7 (2H, m, SiOCH, OCH_2), 4.7-4.9 (2H, m, CH_2CHO). MS m/z: 323 (M^+-CH_3). Anal. Calcd for $C_{17}H_{26}O_5Si$: C, 60.32; H, 7.74. Found C, 60.07; H, 7.81.

(+)-(1*S*,5*S*,9*S*,10*R*,13*S*)-3,12-dioxatetracyclo[8.2.1.0^{5,9}.0^{5,13}]tridecan-4,8,11-trione 13 a) From (-)-11: A solution of (-)-**11** (142 mg, 0.42 mmol), Jones reagent (0.3 mL, 0.8 mmol), and 40% HF (0.02 mL) in acetone (3 mL) was stirred at rt for 19 h. After addition of isopropyl alcohol (IPA) (1 mL), the whole was stirred at rt for 0.5 h, and neutralized with $NaHCO_3$. After filtration and concentration, the residue was taken up into acetone and the insoluble material was again removed by filtration. Concentration and column chromatography (AcOEt-benzene 2:1) afforded (+)-**13** (49 mg, 69%) as colorless needles of mp 188.5-190 °C (AcOEt-hexane). $[\alpha]_D^{20}$ +158 °(c 1.06, acetone). IR (KBr): 1770, 1720 cm^{-1}. NMR δ: 2.0-2.3 (1H, m), 2.50 (1H, dd, J=8, 12 Hz, CH_2), 2.6-2.9, 2.9-3.1 (each 2H m), 3.40 (1H, dt, J=2, 8 Hz, CHCHO), 4.46 (1H, dd, J=14, 2 Hz, OCH_2), 4.7-5.0 (2H, m, OCH_2CHO). MS m/z: 222 (M^+). Anal. Calcd for $C_{11}H_{10}O_5$-1/4H_2O: C, 58.28; H, 4.67. Found C, 58.29; H, 4.47.
b) From (+)-12: Similarly (+)-**12** was converted in 49% yield into (+)-**13** as colorless needles of mp 188-189 °C (AcOEt-hexane). $[\alpha]_D^{20}$ +157 °(c 0.91, acetone).

(+)-(1*S*,5*R*,8*S*,9*S*,10*R*,13*R*)-8-*tert*-Butyldimethylsilyloxy-11-methoxy-11-methyl-3,12-dioxatetracyclo[8.2.1.0^{5,9}.0^{5,13}]tridecan-4-one 15 and (-)-(1*S*,5*S*,8*S*,9*S*,10*R*,13*S*)-8-*tert*-Butyldimethylsilyloxy-4-methoxy-4-methyl-3,12-dioxatetracyclo[8.2.1.0.^{5,9}0^{5,13}]tridecan-11-one 16 A solution of MeLi (1.16 M in ether, 3.32 mL, 3.85 mmol) was added to a solution of (-)-**11** (1.04 g, 3.08 mmol) in THF (170 mL) at -78 °C. The whole was stirred at -78 °C for 30 min, and quenched with satd. NH_4Cl and satd. NaCl. After extraction with CH_2Cl_2 (100 mL x 5), the extract was washed with satd NaCl and dried. After concentration, the residue was dissolved in CH_2Cl_2 (20 mL), $CH(OCH_3)_3$ (2.9 mL, 27 mmol) and pyridinium *p*-toluenesulfonate (PPTS) (45 mg) were added, and the whole was stirred at rt for 17 h. After addition of satd. $NaHCO_3$, the organic layer was separated, and then the water layer was extracted with CH_2Cl_2 (10 mL x 1). The combined organic layer was dried and concentrated.

Chromatography of the residue (AcOEt-hexane 1:10) afforded (-)-**16** (0.30 g, 26%) as colorless needles of mp 122-123 °C (hexane), (-)-**15** (0.67 g, 59%) as a colorless oil, and recovered (-)-**11** (0.19 g, 18% recovery). (-)-**15**: $[\alpha]_D^{20}$ -25.0 °(c 1.12, $CHCl_3$). IR (neat): 1730 cm^{-1}. NMR δ: 0.04 (6H, s, $(C\underline{H}_3)_2$), 0.88 (9H, s, $(CH_3)_3$), 1.43 (3H, s, $C(C\underline{H}_3)OCH_3$), 1.6-2.1 (5H, m), 2.4-2.6 (1H, m), 2.66 (1H, t, J=6 Hz, $C\underline{H}CH(O)CH_2O$), 3.23 (3H, s, $OC\underline{H}_3$), 3.9-4.2 (2H, m, SiOC<u>H</u>, $C\underline{H}(O)CH_2O$), 4.37 (1H, dd, J=2, 13 Hz, $OC\underline{H}_2CHO$), 4.64 (1H, dd, J=3, 13 Hz, $OC\underline{H}_2$). MS m/z: 368 (M^+). HRMS m/z: Calcd for $C_{19}H_{33}O_5Si$ (M^++1): 369.2096. Found 369.2121. (-)-**16**: $[\alpha]_D^{20}$ -41.2 °(c 0.82, $CHCl_3$). IR (neat): 1760 cm^{-1}. NMR δ: 0.05 (6H, s, $(C\underline{H}_3)_2$), 0.84 (9H, s, $(C\underline{H}_3)_3$), 1.24 (3H, s, $C(C\underline{H}_3)OCH_3$), 1.4-1.6 (1H, m), 1.7-2.1 (3H, m), 2.41 (1H, dd, J=4, 7 Hz, C<u>H</u>CO), 2.5-2.7 (2H, m), 3.19 (3H, s, $OC\underline{H}_3$), 3.7-3.9 (2H, m, SiOC<u>H</u>, CHC<u>H</u>O), 4.14 (1H, brs, $OC\underline{H}_2CHO$), 4.60 (1H, dt, J=2, 7 Hz, $OC\underline{H}_2CHO$). MS m/z: 368 (M^+). Anal. Calcd for $C_{19}H_{32}O_5Si$: C, 61.92; H, 8.75. Found C, 62.05; H, 8.93.

(-)-(1*S*,5*S*,8*R*,9*S*,10*R*,13*S*)-8-*tert*-Butyldimethylsilyloxy-11-methoxy-11-methyl-3, 12-dioxatetracyclo[8.2.1.0.^{5,9}0^{5,13}]tridecan-4-one 17 and (-)-(1*S*,5*S*,8*R*,9*S*,10*R*,13*S*)-8-*tert*-butyldimethylsilyloxy-4-methoxy-4-methyl-3,12-dioxatetracyclo[8.2.1.0.^{5,9}0^{5,13}]tridecan-11-one 18 According to the same procedure for **15**, (-)-**17** and (-)-**18** were prepared from (+)-**12** as colorless oils in 7% and 52% yield, respectively. (-)-**17**: $[\alpha]_D^{20}$ -10.5 °(c 0.4, $CHCl_3$). IR (neat): 1720 cm^{-1}. NMR δ: 0.02, 0.04, and 0.07 (6H, 3s, $(C\underline{H}_3)_2$), 0.86 (9H, s, $(C\underline{H}_3)_3$), 1.24, 1.37 (3H, 2s, $C(C\underline{H}_3)OCH_3$), 1.4-2.3 (5H, m), 2.4-2.8 (2H, m), 3.14, 3.24 (3H, 2s, $OC\underline{H}_3$), 3.2-3.3 (1H, m, C<u>H</u>OSi), 4.1-4.8 (3H, m, $C\underline{H}(O)C\underline{H}_2O$). MS m/z: 368 ($M^+$). HRMS m/z: Calcd for $C_{19}H_{32}O_5Si$ (M^+): 368.2020. Found 368.2051. (-)-**18**: $[\alpha]_D^{20}$ -15.7 °(c 0.72, $CHCl_3$). IR (neat): 1770 cm^{-1}. NMR δ: 0.0-0.1 (6H, m, $(C\underline{H}_3)_2$), 0.87 and 0.90 (9H, 2s, $(C\underline{H}_3)_3$), 1.12,1.16 (3H, 2s, $C\underline{H}_3COCH_3$), 1.3-2.3 (5H, m), 3.16 (3H, s, $C(CH_3)OC\underline{H}_3$), 3.4-3.7 (2H, m), 3.6-3.8 (2H, m, SiOC<u>H</u>CHCHCHC<u>H</u>O), 3.9-4.3 (2H, m, $OC\underline{H}_2CHO$). HRMS m/z: Calcd for $C_{19}H_{33}O_5Si$ (M^+): 369.2098. Found 369.2130.

(+)-(1*S*,5*R*,8*R*,9*S*,10*S*,13*S*)-4,11-dimethoxy-3,12-dioxatetracyclo[8.2.1.0.^{5,8}0^{5,13}]tridecan-8-ol 19 DIBAH (1.76 M in hexane, 0.30 mL, 0.53 mmol) was added to a solution of (+)-**12** (60 mg, 0.18 mmol) in THF (6 mL) at -78 °C. The whole was stirred at -78 °C for 1 h. After addition of acetone (1 mL). the mixture was warmed to rt. After concentration, the residue was dissolved in CH_2Cl_2 (5 mL). $CH(OCH_3)_3$ (1 mL) and *p*-toluenesulfonic acid (0.2 g) were added, and the whole was stirred at rt for 30 min. Benzene (20 mL) was added, and the mixture was washed successively with 5% aq. HCl, water, satd. aq. $NaHCO_3$, and satd. aq. NaCl, then dried. Concentration and chromatography (AcOEt-benzene 1:40) gave the acetal (41 mg, 62%) as a colorless oil. $[\alpha]_D^{24}$ +7.13 °(c 1.01, $CHCl_3$). IR (neat): 1140, 1050 cm^{-1}. NMR δ: 0.02, 0.03 (6H, 2s, $(C\underline{H}_3)_2$), 0.87 (9H, s, $(C\underline{H}_3)_3$), 1.5-1.7 (2H, m), 1.7-2.0 (2H, m), 2.27 (1H, dd, J=5, 7 Hz, $C\underline{H}CH(OCH_3)O$), 2.47 (1H, t, J=7 Hz, $OCH_2C\underline{H}CH$), 2.83 (1H, dd, J=5, 7 Hz, $OCHC\underline{H}CH$), 3.36 (6H, s, $OC\underline{H}_3$), 3.7-3.8 (2H, m, SiOC<u>H</u>. CHC<u>H</u>O), 3.9-4.2 (3H, m, $OC\underline{H}_2CHCH$, $C\underline{H}(OCH_3)O$), 4.76 (1H, s, $CC\underline{H}(OCH_3)O$). MS m/z: 370 (M^+). A solution of the acetal (75 mg) and 40% aq HF in MeOH (4 mL) was stirred at rt for 3 h. After neutralization with satd. $NaHCO_3$, the mixture was extracted with CH_2Cl_2 (20 mL x 3), and then the combined organic layer was dried. Concentration afforded **19** (47 mg, 91%) as a colorless oil. $[\alpha]_D^{24}$ 0.00 (c 0.75, $CHCl_3$). IR (neat): 3400 cm^{-1}. NMR δ: 1.4-2.1 (4H, m, $(C\underline{H}_2)_2$), 2.36 (1H, t, J=5 Hz, CHC<u>H</u>CH), 2.52 (1H, t, J=7 Hz, C<u>H</u>), 2.78 (1H, dd, J=5, 7 Hz, C<u>H</u>), 3.32, 3.33 (each 3H, s, $OC\underline{H}_3$), 3.79 (2H, s, OCH_2CHCH), 4.0-4.3 (3H, m, SiOC<u>H</u>CHCHCHC<u>H</u>O, $CC\underline{H}(OCH_3)O$), 4.84 (1H, s). HRMS m/z: Calcd for $C_{13}H_{20}O_5$ (M^+): 256.1311. Found 256.1356.

(-)-(1*S*,5*R*,8*S*,9*S*,10S,13*S*)-8-Benzyloxy-4,11-dimethoxy-3,12-dioxatetracyclo-[8.2.1.0.^{5,8}0^{5,13}]tridecan-8-ol 20 Diethyl azodicarboxylate (DEAD) (0.04 mL, 0.26 mmol) was added to a solution of **19** (47 mg, 0.18 mmol), benzoic acid (35 mg, 0.29 mmol), and triphenylphosphine (84 mg, 0.32 mmol) in THF (1.5 mL), and the whole was stirred at rt for 30 min. After concentration and dilution with MeOH (2 mL), 15% aq. NaOH (0.2 mL, 0.75 mmol) was added, and the whole was stirred at rt for 17 h. After addition of satd. NaCl, the mixture was extracted with CH_2Cl_2 (20 mL x 3), and the combined extracts were dried. Concentration and chromatography (AcOEt-benzene 1:1) afforded 8-hydroxyl compound (45 mg, 96%) as a colorless oil. IR (neat): 3400 cm^{-1}. NMR δ: 1.50-2.80 (8H, m), 3.30 (3H, s, $OC\underline{H}_3$), 3.32 (3H, s, $OC\underline{H}_3$), 3.70-3.90 (2H, m), 3.9-4.2 (2H, m, $CH(O)C\underline{H}_2$), 4.25 (1H, s, $C\underline{H}(OMe)O$), 4.83 (1H, s, $C\underline{H}(OMe)O$). MS m/z: 2256 (M^+). A solution of the alcohol (22 mg, 0.086 mmol) in DMF (0.4 mL) was added to a suspension of NaH (50% in oil, 10 mg, 0.21 mmol) in DMF (0.1 mL). Benzyl bromide (0.02 mmol, 0.17 mmol) was added, and the mixture was stirred at rt for 1.5 h. After addition of satd. NaCl, the mixture was extracted with CH_2Cl_2 (10 mL x 3), and the combined extracts were dried. Concentration and chromatography (ether-benzene 1:15) gave (-)-**20** (26 mg, 87%) as

a colorless oil. $[\alpha]_D^{20}$ -24.6 °(c 1.13, $CHCl_3$). IR (neat): 1150, 1050 cm^{-1}. NMR δ: 1.54-2.24 (5H, m), 2.4-2.6 (2H, m), 3.32 (3H, s, OCH_3), 3.34 (3H, s, OCH_3), 3.7-3.9 (3H, m, $CH(O)CH_2$), 4.12 (1H, d, J=7 Hz, OCH), 4.26 (1H, s, CH(OMe)O), 4.41 (1H, d, J=12 Hz, $C_6H_5CH_2$), 4.44 (1H, d, J=12 Hz, $C_6H_5CH_2$), 4.88 (1H, s, CH(OMe)O), 7.16 (5H, s, C_6H_5). HRMS m/z: Calcd for $C_{20}H_{26}O_5$ (M^+): 346.1778. Found 346.1723.

(-)-(1*S*,5*R*,8*S*,9*S*,10*S*,13*S*)-8-Benzyloxy-3,12-dioxatetracyclo[8.2.1.0.^{5,9}0^{5,13}]tridecan-4,11-dione 21 A solution of (-)-**20** (189 mg, 0.55 mmol) in AcOH (8 mL), water (8 mL), and THF (20 mL) was heated under reflux for 18 h, and then concentrated. The residue was dissolved in acetone (5 mL), and then Jones reagent (0.4 mL, 1.1 mmol) was added. The mixture was stirred at rt for 1 h, and then quenched with IPA. After addition of 10% aq. HCl, the mixture was extracted with $CHCl_3$ (20 mL x 3), the combined extracts were dried. Concentration gave (-)-**21** (169 mg, 99%) as colorless needles of mp 208-209 °C (AcOEt). $[\alpha]_D^{24}$ -51.9 °(c 0.54, $CHCl_3$). IR (KBr): 1770, 1720 cm^{-1}. NMR δ: 1.7-2.7 (5H, m), 2.8-3.1 (2H, m), 3.98 (1H, d, J=4 Hz, $C_6H_5CH_2OCH$), 4.3-4.5 (1H, m, $CH(O)CH_2$), 4.46 (1H, d, J=11 Hz, $CH(O)CH_2$), 4.56 (1H, d, J=11 Hz, $CH(O)CH_2$), 4.6-4.9 (2H, m, $C_6H_5CH_2$), 7.31 (5H, s, C_6H_5). MS m/z: 314 (M^+). Anal. Calcd for $C_{18}H_{18}O_5$: C, 68.78; H, 5.77. Found C, 68.54; H, 5.80.

(-)-(1*S*,5*R*,8*S*,9*S*,10*S*,13*S*)-8-Benzyloxy-11-methoxy-11-methyl-3,12-dioxatetracyclo-[8.2.1.0.^{5,9}0^{5,13}]tridecan-4-one 22 a) From (-)-21: MeLi (1.90 M in ether, 0.16 mL, 0.22 mmol) was added to a stirred solution of (-)-**21** (89 mg, 0.28 mmol) in THF (10 mL) at -78 °C, and the whole was stirred at -78 °C for 25 min, and then quenched with satd. NH_4Cl and satd. NaCl. The mixture was extracted with AcOEt (15 mL x 5). The combined extracts were washed with satd. NaCl, dried, and then concentrated. A solution of this residue, $CH(OCH_3)_3$ (2 mL), and PPTS (20 mg) in CH_2Cl_2 (5 mL) was stirred at rt for 16 h. After addition of satd. $NaHCO_3$, the mixture was extracted with CH_2Cl_2 (10 mL x 3), and the combined extracts were dried. Concentration and chromatography (AcOEt-hexane 1:2) afforded (-)-**22** (24 mg, 25%) as a colorless oil and recovered (-)-**21** (67 mg, 75% recovery). $[\alpha]_D^{22}$ -9.83 °(c 1.20, $CHCl_3$). IR (neat): 1730 cm^{-1}. NMR δ: 1.43 (2.6H, s, CH_3), 1.55 (0.4 H, s, CH_3), 1.7-2.9 (7H, m), 3.24 (2.6H, s, OCH_3), 3.48 (0.4H, s, OCH_3), 3.88 (1H, d, J=4 Hz, $C_6H_5CH_2OCH$), 4.15 (1H, dt, J=6, 2 Hz, OCH_2CHO), 4.41 (1H, dd, J=13, 2 Hz, OCH_2CHO), 4.52 (2H, s, $C_6H_5CH_2$), 4.68 (1H, dd, J=13, 2 Hz, OCH_2), 7.1-7.5 (5H, m, C_6H_5). HRMS m/z: Calcd for $C_{20}H_{24}O_5$ (M^+): 344.1621. Found 344.1551.
b) From (-)-15: A solution of (-)-**15** (0.67 g) and 40% aq. HF in MeOH (15 mL) was stirred at rt for 5 h. After addition of satd. $NaHCO_3$ and concentration, the residue was taken up into satd. NaCl, and extracted with $CHCl_3$ (50 mL x 3). The combined extracts were dried. Concentration gave desilylated **15** (344 mg, 74%) as colorless solid of mp 174-175 °C. $[\alpha]_D^{20}$ -6.36 °(c 0.66, $CHCl_3$). IR (KBr): 3480, 1690 cm^{-1}. NMR δ: 1.43 (3H, s, $C(CH_3)OCH_3$), 1.6-2.3 (4H, m), 2.3-2.7 (4H, m), 3.17 (3H, s, OCH_3), 4.06 (2H, br, OCH_2CHO, CHOH), 4.40 (1H, dd, J=2, 12 Hz, OCH_2CHO), 4.64 (1H, dd, J=2, 12 Hz, OCH_2CHO). MS m/z: 254 (M^+). HRMS m/z: Calcd for $C_{13}H_{18}O_5$ (M^+): 254.1154. Found 254.1211. A solution of desilylated (-)-**15** (344 mg, 1.35 mmol) in DMF (4 mL) was added to a stirred suspension of NaH (50% in oil, 105 mg, 2.2 mmol) in DMF (1 mL) at 0 °C and the whole was stirred at rt for 1 h. Benzyl bromide (0.24 mL, 2.1 mmol) was added to the mixture at 0 °C and the whole was stirred at rt for 16 h. After addition of satd. NH_4Cl, the mixture was extracted with CH_2Cl_2 (10 mL x 4). The combined extracts were successively washed with 10% HCl, water, and satd. $NaHCO_3$, then dried. Concentration and chromatography (AcOEt-hexane 1:3) afforded (-)-**22** (0.39 g, 77%) as a colorless oil. $[\alpha]_D^{20}$ -10.2 °(c 1.24, $CHCl_3$).

(+)-(1*S*,2*S*,6*S*,7*S*,8*S*)-8-Benzyloxy-3-hydroxymethyl-5-methoxy-1,5-dimethyl-4-oxatricyclo-[5.3.0.0^{2,6}]decane 23 DIBAH (1.76 M in hexane, 0.99 mL, 1.74 mmol) was added to a solution of (-)-**22** (380 mg, 1.1 mmol) in toluene (20 mL) at -78 °C, and the whole was stirred at -78 °C for 1 h, and 15% NaOH (10 mL) was added. After extraction with ether (50 mL x 3), the combined extracts were washed with satd. NaCl and dried. Concentration gave hemiacetal (0.38 g, quant.) as a colorless oil. $[\alpha]_D^{20}$ +23.3 °(c 0.55, $CHCl_3$). IR (neat): 3400 cm^{-1} NMR d: 1.39 (3H, s, $C(CH_3)OCH_3$), 1.5-2.3 (6H, m), 2.42-2.77 (2H, m,), 3.19 (3H, s, OCH_3), 3.5-4.2 (4H, m, OCH_2CHO, $CHOCH_2C_6H_5$), 4.3-4.8 (3H, m, HOCHO, $CH_2C_6H_5$), 7.20 (5H, s, C_6H_5). HRMS m/z: Calcd for $C_{20}H_{26}O_5$ (M^+): 346.1781. Found 346.1803. A solution of the hemiacetal (0.38 g, 1.1 mmol), 80% N_2H_4 H_2O (2 mL), and KOH (300 mg) in diethylene glycol (10 mL) was heated at 140 °C for 70 min, allowed to warm up to 200 °C during 30 min, and heated at 200 °C for 1 h, then cooled to rt. After addition of satd. NaCl, the mixture was extracted with ether (30 mL x 5). Combined extracts were washed with satd. NaCl, then dried. Concentration and chromatography (AcOEt-benzene 1:3) gave (+)-**23** (192 mg, 53%) as a colorless oil. $[\alpha]_D^{20}$ +51.7 °(c 1.04, $CHCl_3$). IR (neat): 3450 cm^{-1}. NMR δ: 1.16 (3H, s, CH_3), 1.39 (3H, s, $C(CH_3)OCH_3$), 1.4-2.4 (8H, m), 3.14 (3H, s, OCH_3), 3.5-3.8

(2H, m, $HOC\underline{H}_2CHO$), 3.8-4.2 (2H, m, $HOCH_2C\underline{H}O$, $C\underline{H}OCH_2C_6H_5$), 4.38 (2H, s, $C\underline{H}_2C_6H_5$), 7.22 (5H, s, $C_6\underline{H}_5$). MS m/z: 301 (M^+-OCH_3). HRMS m/z: Calcd for $C_{13}H_{25}O_3$ (M^+-OCH_3): 301.1804. Found 301.1834.

(+)-(1*S*,4*S*,5*S*)-6,7-Diacetyl-4-benzyl-1-methylbicyclo[3.2.0]heptane 24 A solution of (+)-**23** (28 mg) and 10% H_2SO_4 (0.05 mL) in 50% aq. THF (1 mL) was stirred at 0 °C for 30 min. To this solution was added 15% NaOH (0.07 mL) and $NaBH_4$ (10 mg, 0.26 mmol), and the mixture was stirred at 0 °C for 1.5 h, and acetone (1 mL) was added. The mixture was concentrated, then water (1 mL), AcOEt (1 mL), and $NaIO_4$ (80 mg) was added to the residue. After stirring at rt for 2 h, the mixture was taken up into AcOEt (20 mL), washed with water, 10% $Na_2S_2O_3$, and satd. NaCl, successively, then dried, and then concentrated. A solution of MeLi (0.93 M in ether, 1.4 mL, 1.3 mmol) was added to a solution of the residue in ether (0.5 mL), and the whole was stirred at rt for 2 h. After addition of satd. NH_4Cl and satd. NaCl, the mixture was extracted with CH_2Cl_2 (20 mL x 3). The combined extracts were dried, and concentrated to give an oil (30 mg). This oil was dissolved in acetone (1 mL). Jones reagent (0.1 mL, 0.17 mmol) was added at 0 °C. The whole was stirred at 0 °C for 2 h, and IPA (1 mL) was added. After neutralization with satd. $NaHCO_3$ and filtration, the mixture was diluted with CH_2Cl_2 (10 mL) and washed with satd. NaCl, and then dried. Concentration and chromatography (AcOEt-benzene 1:15) afforded (+)-**24** (17 mg, 67%) as a colorless oil $[\alpha]_D^{20}$ +5.0 °(c 1.60, $CHCl_3$). IR (neat): 1710 cm^{-1}. NMR δ: 1.20 (3H, s, $C\underline{H}_3$), 1.6-2.3 (4H, m), 2.05 (3H, s, $C\underline{H}_3CO$), 2.09 (3H, s, $C\underline{H}_3CO$), 2.46 (1H, dd, J=6, 9 Hz, $C\underline{H}Ac$), 2.97 (1H, d, J=6 Hz, $C\underline{H}CHO$), 3.44 (1H, d, J=9 Hz, $AcC\underline{H}CHAc$), 3.72 (1H, br, $C\underline{H}OCH_2C_6H_5$), 4.42, 4.54 (each 1H, d, J=12 Hz, $C\underline{H}_2C_6H_5$), 7.24 (5H, s, $C_6\underline{H}_5$). HRMS m/z: Calcd for $C_{13}H_{24}O_3$ (M^+): 300.1723. Found 300.1718.

(-)-(1*S*,2*S*,6*S*,7*S*,8*S*)-8-Benzyloxy-1,5-dimethyltricyclo[5.3.0.0^{2,6}]dec-4-en-3-one 25 A solution of (+)-**24** (96 mg, 0.32 mmol) and $KOBu^t$ (53 mg, 0.41 mmol) in *tert*-BuOH (1.4 mL) was heated at 75 °C for 10 min. After addition of water, the mixture was extracted with CH_2Cl_2 (10 mL x 3) and the combined extracts were dried. Concentration and chromatography (ether) afforded (-)-**25** (77 mg, 85%) as a colorless oil. $[\alpha]_D^{20}$ -227 °(c 0.97, $CHCl_3$). IR (neat): 1685, 1610 cm^{-1}. NMR δ: 1.16 (3H, s, $C\underline{H}_3$), 1.4-2.3 (5H, m), 2.10 (3H, s, $C\underline{H}_3C{=}C$), 2.3-2.6 (2H, m), 3.85 (1H, d, J=3 Hz, $C\underline{H}O$), 4.50 (2H, s, $C\underline{H}_2$), 6.00 (1H, br, $C{=}C\underline{H}O$), 7.31 (5H, s, $C_6\underline{H}_5$). HRMS m/z: Calcd for $C_{13}H_{22}O_2$ (M^+): 282.1620. Found 282.1622.

(-)-(1*S*,2*S*,5*R*,6*S*,7*S*,8*S*)-8-Hydroxy-1,5-dimethyltricyclo[5.3.0.0^{2,6}]decan-3-one 26 A solution of (-)-**25** (10 mg) in ether (2 mL) was hydrogenated over 5% Pd-C (2 mg) under an H_2 at rt for 3 h. Filtration and concentration give (-)-**26** (7 mg, quant.) as colorless prisms of mp 113.5-115 °C (ether-hexane). $[\alpha]_D^{20}$ -325 °(c 0.96, $CHCl_3$). IR (neat): 3440, 1700 cm^{-1}. NMR δ: 1.11 (3H, s, $C\underline{H}_3$), 1.11 (3H, d, J=6 Hz, $C\underline{H}_3$), 1.5-2.7 (11H, m), 4.08 (1H, d, J=3 Hz, $C\underline{H}OH$). MS m/z: 194 (M^+). Anal. Calcd for $C_{12}H_{18}O_2$ $1/8H_2O$: C, 73.33; H, 9.36. Found C, 73.15; H, 9.34.

(+)-(1*R*,2*S*,6*R*,7*S*,10*R*)-6,10-dimethyltricyclo[5.3.0.0^{2,6}]decan-3-one 27 A solution of (-)-**26** (16 mg, 0.082 mmol), 80% $N_2H_4{\cdot}H_2O$ (0.2 mL), and KOH (22 mg) in triethylene glycol (0.5 mL) was heated at 140 °C for 1.5 h and allowed to warm up to 210 °C during 30 min, and heated at 210 °C for 3.5 h. After addition of water, the mixture was extracted with ether (10 mL x 5). The combined extracts were washed with satd. NaCl and dried. Concentration and chromatography gave the corresponding alcohol (8 mg, 54%) as a colorless oil. $[\alpha]_D^{20}$ +16.9 °(c 0.70, $CHCl_3$). IR (neat): 3360 cm^{-1}. NMR δ: 0.95 (3H, d, J=6 Hz, $C\underline{H}_3$), 1.02 (3H, s, $C\underline{H}_3$), 1.1-2.2 (13H, m), 3.94 (1H, d, J=3 Hz, $C\underline{H}OH$). MS m/z: 180 (M^+). HRMS m/z: Calcd for $C_{12}H_{20}O$: 180.1511. Found 180.1500. Jones reagent (0.04 mL, 0.067 mmol) was added to the alcohol (6 mg, 0.033 mmol) in acetone (0.5 mL) at 0 °C and the mixture was stirred at 0 °C for 50 min. After addition of IPA (0.1 mL) and satd. $NaHCO_3$, the mixture was extracted with CH_2Cl_2 (10 mL x 3). The combined extracts were dried, and concentrated to afford (+)-**27** (6 mg, quant.) as a colorless oil. $[\alpha]_D^{20}$ +121 °(c 0.60, $CHCl_3$). IR (neat): 1735 cm^{-1}. NMR δ: 0.99 (3H, s, $C\underline{H}_3$), 1.00 (3H, d, J=6 Hz, $C\underline{H}_3$), 1.1-2.2 (9H, m), 2.3-2.8 (3H, m, $C\underline{H}COC\underline{H}_2$). HRMS m/z: Calcd for $C_{12}H_{18}O$: 178.1358. Found 178.1368.

(+)-(1*R*,2*S*,6*S*,7*S*,10*R*)-6,10-dimethyltricyclo[5.3.0.0^{2,6}]dec-4-en-3-one 28 A solution of (+)-**27** (23 mg, 0.13 mmol) and phenylselenyl chloride (27 mg, 0.14 mmol) in AcOEt (1 mL) was stirred at rt for 45 min and then concentrated. After addition of $NaHCO_3$ (15 mg), water (0.3 mL), MeOH (3 mL), and $NaIO_4$ (100 mg), the whole was stirred at rt for 1.5 h. The mixture was filtrated and diluted with CH_2Cl_2 (20 mL), and then washed with satd. NaCl, and dried. Concentration and chromatography (AcOEt-hexane 1;5) afforded **28** (10 mg, 42%) as a pale yellow oil. $[\alpha]_D^{20}$ +214 °(c 1.78, $CHCl_3$). IR (neat): 1700, 1580

cm^{-1}. NMR δ: 1.06 (3H, s, CH_3), 1.07 (3H, d, J=7 Hz, CH_3), 1.2-2.6 (8H, m), 6.16, 7.51 (each 1H, d, J=7 Hz, CH=CH). HRMS m/z: Calcd for $C_{12}H_{16}O$ (M^+): 176.1199. Found 176.1186.

(-)-(1*R*,2*S*,3*R*,6*R*,7*S*,10*R*)-6,10-Dimethyltricyclo[5.3.0.0^{2,6}]dec-4-en-3-ol 29 DIBAH (1.8 M in hexane, 3.3 mL, 5.8 mmol) was added to a stirred solution of (+)-**28** (400 mg, 2.3 mmol) in ether (10 mL) at -78 °C, and the whole was stirred at -78 °C for 50 min. After addition of 15% NaOH, the mixture was extracted with ether (30 mL x 3). The combined extracts were washed with satd. NaCl and dried. Concentration afforded (-)-**29** (403 mg, quant.) as colorless needles of mp 134-135 °C (hexane). $[\alpha]_D^{18}$ -68.8 °(c 1.02, $CHCl_3$). IR (KBr): 3400, 1610 cm^{-1}. NMR δ: 0.93 (3H, s, CH_3), 0.94 (3H, d, J=6 Hz, CH_3), 1.1-2.0 (6H, m), 2.0-2.4 (2H, m), 2.58 (1H, q, J=6 Hz), 5.17 (1H, tt, J=7, 1 Hz, CHOH), 5.60, 5.72 (each 1H, dd, J=5, 1 Hz, CH=CH). MS m/z: 178 (M^+). Anal. Calcd for $C_{12}H_{18}O$: C, 80.85; H, 10.18. Found C, 80.74; H, 10.48.

(+)-(1*R*,2*S*,3*S*,6*R*,7*S*,10*R*)-6,10-Dimethyltricyclo[5.3.0.0^{2,6}]dec-4-en-3-ol 30 A solution of (-)-**29** (403 mg, 2.3 mmol), triphenylphosphine (0.90 g, 3.44 mmol), benzoic acid (0.42 g, 3.44 mmol), and DEAD (0.54 mL, 3.44 mmol) in THF (8 mL) was stirred at 0 °C for 5 h and then concentrated. The residue was dissolved in ether, and washed with satd. $NaHCO_3$ and satd. NaCl, successively, then dried, then concentrated. The residue and 15% NaOH (2 mL, 7.5 mmol) in MeOH (17 mL) was stirred at rt for 13 h. After concentration, the residue was dissolved in ether, washed with satd. NaCl, and then dried. Concentration and chromatography (ether-hexane 1:20) gave (+)-**30** (310 mg, 71%) as colorless needles of mp 89.5-90.5 °C (hexane). $[\alpha]_D^{19}$ +83.4 °(c 0.35, $CHCl_3$). IR (KBr): 3200 cm^{-1}. NMR δ: 1.01 (3H, d, J=6 Hz, CH_3), 1.01 (3H, s, CH_3), 1.1-2.1 (8H, m), 2.25 (1H, t, J=6 Hz), 4.36 (1H, d, J=2 Hz, CHOH), 5.83 (1H, ddd, J=5, 2, 1 Hz, CH=CHCHOH), 5.91 (1H, d, J=5 Hz, CH=CHCHOH). Ms m/z: 178 (M^+). Anal. Calcd for $C_{12}H_{18}O \cdot 1/10H_2O$: C, 80.03; H, 10.19. Found C, 80.08; H, 10.31.

(+)-(1*R*,2*S*,3*R*,4*R*,5*S*,6*R*,7*S*,10*R*)-4,5-Epoxy-6,10-dimethyltricyclo[5.3.0.0^{2,6}]decan-3-ol 31 A solution of (+)-**30** (350 mg, 2.1 mmol) and MCPBA (70%, 0.81 g, 3.3 mmol) in CH_2Cl_2 (20 mL) was stirred at rt for 18 h and then concentrated. The residue was diluted with ether (100 mL) and washed with satd. $Na_2S_2O_3$, satd. $NaHCO_3$, and satd. NaCl, then dried. Concentration and chromatography (ether-benzene 1:20) gave (+)-**30** (336 mg, 81%) as colorless needles of mp 77-79 °C (hexane). $[\alpha]_D^{19}$ +78.2 °(c 1.02, $CHCl_3$). IR (KBr): 3340 cm^{-1}. NMR δ: 0.95 (3H, d, J=6 Hz, CH_3), 1.05 (3H, s, CH_3), 1.1-2.3 (8H, m), 3.40 (1H, t, J=2 Hz, CH(O)CHCHOH), 3.82 (1H, br, CH(O)CHCHOH), 3.95 (1H, d, J=3 Hz, CHOH), 4.07 (1H, br, OH). MS m/z: 194 (M^+). Anal. Calcd for $C_{12}H_{18}O_2 \cdot 1/5\ H_2O$: C, 72.84; H, 9.37. Found C, 72.99; H, 9.28.

(-)-(1*R*,2*S*,3*S*,5*R*,6*R*,7*S*,10*R*)-5-Methoxymethyl-6,10-dimethyltricyclo[5.3.0.0^{2,6}]decan-3-ol 32 A solution of (+)-**31** (306 mg, 1.58 mmol) and PPTS (70 mg) in isopropenyl methyl ether (5 mL) was stirred at rt for 1 h. After addition of satd. $NaHCO_3$, the mixture was extracted with CH_2Cl_2 (20 mL x 3). The extracts were dried over K_2CO_3 and then concentrated. The residue and lithium aluminum hydride (160 mg, 4.2 mmol) in ether (10 mL) was stirred at rt for 2 h.. After successive addition of water (0.15 mL), 15% aq. NaOH (0.16 mL), water (0.48 mL), and K_2CO_3 (solid), the precipitate was filtered off, and the filtrate was concentrated. A solution of the residue, chloromethyl methyl ether (1.5 mL), and diisopropylethylamine (5 mL) in CH_2Cl_2 was stirred at rt for 42 h. After dilution with CH_2Cl_2 (60 mL), the mixture was washed with 5% HCl, water, and satd. $NaHCO_3$, then dried. Concentration and chromatography (AcOEt-hexane 1:5) afforded (-)-**32** (314 mg, 83%) as a colorless oil. $[\alpha]_D^{20}$ -22.4 °(c 1.00, $CHCl_3$). IR (neat): 3400 cm^{-1}. NMR δ: 0.92 (3H, d, J=7 Hz, CH_3), 1.03 (3H, s, CH_3), 1.1-2.4 (10 H, m), 2.85 (1H, br), 3.33 (3H, s, OCH_3), 3.70 (1H, d, J=4 Hz, $CHOCH_2$), 3.6-3.9 (1H, m, CHOH), 4.50, 4.64 (each 1H, d, J=7 Hz, OCH_2O). MS m/z: 240 (M^+). HRMS m/z: Calcd for $C_{14}H_{23}O_3$ (M^+-H): 239.1644. Found 239.1597.

(-)-(1*R*,2*S*,3*S*,5*R*,6*R*,7*S*,10*R*)-5-Methoxymethoxy-6,10-dimethyltricyclo[5.3.0.0^{2,6}]decan-3-yl *p*-toluenesulfonate 33 A solution of (-)-**32** (310 mg, 1.3 mmol) and *p*-toluenesulfonyl chloride (1.2 g, 6.5 mmol) in pyridine (10 mL) was stirred at rt for 69 h. After addition of water (50 mL), the mixture was successively washed with 10% HCl, water, and satd. $NaHCO_3$, then dried. Concentration gave (-)-**33** (507 mg, quant.) as a colorless oil. $[\alpha]_D^{20}$ -21.7 °(c 1.45, $CHCl_3$). IR (neat): 1600, 1355, 1175 cm^{-1}. NMR δ: 0.69 (3H, d, J=6 Hz, CH_3), 0.90 (3H, s, CH_3), 1.0-2.1 (10H, m), 2.37 (3H, s, CH_3Ar), 3.28 (3H, s, OCH_3), 3.67 (1H, dd, J=3, 4 Hz, CH), 4.45, 4.52 (each 1H, d, J=7 Hz, OCH_2O), 4.3-4.7 (1H, m, CHOTs), 7.24 (2H, d, J=8 Hz, Ar), 7.68 (2H, d, J=8 Hz, Ar). HRMS m/z: Calcd for $C_{12}H_{30}O_5S$ (M^+): 394.1814. Found 394.1839.

(-)-Diethyl ((1*S*,2*R*,3*R*,5*R*,6*R*,7*S*,10*R*)-5-methoxymethoxy-6,10-dimethyltricyclo-[5.3.0.0^{2,6}]decan-3-ylmalonate 34 Diethyl malonate (2.2 mL) was added to a stirred suspension of NaH (50% in oil, 700 mg, 15 mmol) in DME (10 mL) at 0 °C, then a solution of (-)-**33** (507 mg, 1.3 mmol) in DME (20 mL) was added, and the whole was heated under reflux for 54 h. After dilution with CH_2Cl_2 (100 mL), the mixture was successively washed with 5% HCl, water, satd. $NaHCO_3$, and satd. NaCl, then dried. Concentration and chromatography (AcOEt-benzene 1:10) afforded (-)-**34** (237 mg, 45%) and recovered (-)-**33** (125 mg, 25% recovery). $[\alpha]_D^{23}$ -54.4 °(c 0.64, $CHCl_3$). IR (neat): 1750, 1730 cm^{-1}. NMR δ: 0.80 (3H, d, J=6 Hz, C<u>H</u>$_3$), 0.96 (3H, s, C<u>H</u>$_3$), 1.24, 1.27 (each 3H, t, J=7 Hz, C<u>H</u>$_3$CH$_2$), 1.6-2.1 (10 H, m), 2.6-3.1 (1H, m), 3.34 (3H, s, OC<u>H</u>$_3$), 3.26 (1H, d, J=11 Hz, CHC<u>H</u>(CO$_2$Et)$_2$), 3.58 (1H, d, J=4 Hz, C<u>H</u>O), 4.15 (2H, q, J=7 Hz, CH$_3$C<u>H</u>$_2$), 4.20 (2H, q, J=7 Hz, CH$_3$C<u>H</u>$_2$), 4.54, 4.64 (each 1H, d, J=8 Hz, OC<u>H</u>$_2$O). HRMS m/z: Calcd for $C_{21}H_{34}O_6$ (M$^+$): 382.2353. Found 382.2353.

(-)-(1*S*,2*R*,3*R*,5*R*,6*R*,7*S*,8*R*)-5-(1-Hydroxyprop-2-en-2-yl)-3-methoxymethoxy-2,8-dimethyltricyclo[5.3.0.0^{2,6}]decane 35 *n*-BuLi (1.50 M in hexane, 0.68 mL, 1.02 mmol) was added to a solution of diisopropylamine (0.15 mL, 1.04 mmol) in DME (2 mL) at -78 °C, and the mixture was stirred at -78 °C for 20 min. A solution of (-)-**34** (273 mg, 0.71 mmol) in DME (4 mL) was added to the mixture at 0 °C, and the whole was stirred at 0 °C for 10 min, and then Vitride (3.5 M in toluene, 1.09 mL, 3.8 mmol) was added. The whole was heated under reflux for 2.5 h. After successive addition of acetone (0.5 mL), ether (6 mL), and water (0.7 mL) at 0 °C, the precipitate was filtered off. Concentration and chromatography (AcOEt-benzene 1:7) gave (-)-**35** (177 mg, 88%) as a colorless oil. $[\alpha]_D^{23}$ -60 °(c 0.3, $CHCl_3$). IR (neat): 3100 1645 cm^{-1}. NMR δ: 0.80 (3H, d, J=6 Hz, C<u>H</u>$_3$), 0.92 (3H, s, C<u>H</u>$_3$), 1.0-2.1 (10H, m), 2.6-3.0 (1H, m, C<u>H</u>C(CH$_2$)CH$_2$OH), 3.28 (3H, s, OC<u>H</u>$_3$), 3.54 (1H, d, J=4 Hz, C<u>H</u>OCH$_2$OCH$_3$), 3.94 (2H, s, C<u>H</u>$_2$OH), 4.48, 4.60 (each 1H, d, J=7 Hz, OC<u>H</u>$_2$O), 4.83 (1H, br, C=C<u>H</u>$_2$), 5.09 (1H, br, C=C<u>H</u>$_2$). HRMS m/z: Calcd for $C_{17}H_{28}O_3$ (M$^+$): 280.2038. Found 280.2049.

(-)-(1*S*,2*R*,3*R*,5*R*,6*R*,7*S*,8*R*)-3-(1-Bromoprop-2-en-2-yl)-5-methoxymethoxy-6,10-dimethyltricyclo[5.3.0.0^{2,6}]decane 36 A solution of (-)-**35** (120 mg, 0.43 mmol) and methanesulfonyl chloride (0.08 mL, 1.03 mmol) in 2,6-lutidine (1 mL) was stirred at 0 °C for 4 h, and diluted with benzene (30 mL). After successive washing with 5% HCl, water, satd. $NaHCO_3$, and satd. NaCl, the organic layer was dried. Concentration afforded mesylate of (-)-**35** (158 mg, quant) as a yellow oil. A solution of the mesylate (185 mg, 0.43 mmol) and lithium bromide (350 mg, 4.0 mmol) in DMF (1 mL) was heated at 50 °C for 30 min. After dilution with benzene (30 mL), the mixture was successively washed with water and satd. NaCl, then dried. Concentration and chromatography (benzene) gave (-)-**36** (133 mg, 90%) as a colorless oil. $[\alpha]_D^{25}$ -24 °(c 0.15, $CHCl_3$). IR (neat): 1635 cm^{-1}. NMR δ: 0.86 (3H, d, J=6 Hz, C<u>H</u>$_3$), 1.00 (3H, s, C<u>H</u>$_3$), 1.2-2.0 (9H, m), 2.14 (1H, dt, J=3, 13 Hz, OCHC<u>H</u>$_2$), 3.1-3.4 (1H, m, C<u>H</u>C(CH$_2$Br)=CH$_2$), 3.36 (3H, s, OC<u>H</u>$_3$), 3.63 (1H, d, J=3 Hz, C<u>H</u>O), 3.89 (2H, s, C<u>H</u>$_2$Br), 4.57, 4.68 (each 1H, d, J=7 Hz, OC<u>H</u>$_2$O), 5.00 (1H, t, J=1 Hz, C=C<u>H</u>$_2$), 5.28 (1H, br, C=C<u>H</u>$_2$). MS m/z: 283, 281 (M$^+$-OCH$_2$OCH$_3$). HRMS m/z: Calcd for $C_{16}H_{24}O_2Br$ (M$^+$-CH$_3$): 329.0941. Found 329.0943.

(-)-(1*S*,2*R*,3*R*,5*R*,6*R*,7*S*,8*R*)-3-Methoxymethoxy-2,8-dimethyl-5-(6-methyl-3-phenylthiohept-1,5-dien-2-yl)tricyclo[5.3.0.0^{2,6}]decane 37 *n*-BuLi (1.5 M in hexane, 0.38 mL, 0.57 mmol) was added to a solution of phenyl prenyl sulfide (0.10 mL, 0.58 mmol) in THF (2.5 mL) at -78 °C, and the whole mixture was stirred at -78 °C for 20 min. A solution of (-)-**36** (120 mg, 0.35 mmol) in THF (2.5 mL) was added to this mixture, and stirred at -78 °C for 25 min. After addition of satd. NH_4Cl, the mixture was extracted with CH_2Cl_2 (15 mL x 3), and the combined extracts were dried. Concentration and chromatography (benzene-hexane 1:2) gave (-)-**37** (72 mg, 46%) as a colorless oil. $[\alpha]_D^{25}$ -26.4 °(c 0.84, $CHCl_3$). IR (neat): 3100 1640 cm^{-1}. NMR δ: 0.6-0.9 (3H, m, C<u>H</u>$_3$), 0.97 (3H, s, C<u>H</u>$_3$), 1.1-2.5 (18H, m), 2.7-3.0 (1H, m), 3.31 (1.5H, s, OC<u>H</u>$_3$), 3.32 (1.5H, s, OC<u>H</u>$_3$), 3.57 (1H, d, J=4 Hz, C<u>H</u>O), 3.9-4.2 (1H, m, C<u>H</u>SPh), 4.4-5.1 (5H, m, C=C<u>H</u>$_2$, C=C<u>H</u>, OC<u>H</u>$_2$O), 7.1-7.5 (5H, m, C$_6$<u>H</u>$_5$). HRMS m/z: Calcd for $C_{28}H_{40}O_2S$ (M$^+$): 440.2749. Found 440.2783.

(-)-(1*S*,2*R*,3*R*,5*R*,6*R*,7*S*,8*R*)-3-Methoxymethoxy-2,8-dimethyl-5-(6-methylhept-1,5-dien-2-yl)tricyclo[5.3.0.0^{2,6}]decane 38 Lithium (30 mg, 4.3 mmol) was added to ethylamine (10 mL) at -78 °C. To a blue colored solution was added a solution of (-)-**37** (70 mg, 0.16 mmol) in ether (2 mL), and the mixture was stirred at -78 °C for 25 min. After addition of satd. NH_4Cl, the mixture was extracted with ether (15 mL x 3). The combined extracts were washed with satd. NaCl, and then dried. Concentration and chromatography (benzene-hexane 1:3) gave (-)-**38** (38 mg, 72%) as a colorless oil. $[\alpha]_D^{21}$ -10.2 °(c 0.55, $CHCl_3$). IR (neat): 3100, 1640 cm^{-1}. NMR δ: 0.86 (3H, d, J=6 Hz, C<u>H</u>$_3$), 0.99 (3H, s, C<u>H</u>$_3$), 1.2-2.1

(13H, m), 1.60 (3H, s, C$\underline{H}_3$), 1.67 (3H, s, C$\underline{H}_3$), 2.13 (1H, dt, J=3, 14 Hz, C$\underline{H}_2$), 2.7-3.0 (1H, m, C$\underline{H}$), 3.36 (3H, s, OC$\underline{H}_3$), 3.60 (1H, d, J=3 Hz, C$\underline{H}$O), 4.55 and 4.67 (each 1H, d, J=7 Hz, OC$\underline{H}_2$O), 4.83 (1H, br, C=C$\underline{H}_2$), 4.74 (1H, br, C=C$\underline{H}_2$), 5.11 (1H, t, J=7 Hz, C$\underline{H}$=C). HRMS m/z: Calcd for $C_{22}H_{36}O_2$ (M^+): 332.2715. Found 332.2735.

(+)-Stoechospermol 2 A solution of (-)-**38** (11 mg) and 10% HCl (0.1 mL) in MeOH (2 mL) was heated at 50 °C for 4 h. Concentration and chromatography (benzene) gave (+)-**2** (6.8 mg, 71%) as a colorless solid of mp 64-64.5 °C. $[\alpha]_D^{22}$ +39.1 °(c 1.13, $CHCl_3$). $[\alpha]_D^{27}$ +38.5 °(c 0.47, EtOH). IR ($CHCl_3$): 3600, 3080, 1640 cm^{-1}. NMR δ: 0.86 (3H, d, J=6 Hz, C$\underline{H}_3$), 0.99 (3H, s, C$\underline{H}_3$), 1.2-1.7 (4H, m), 1.60 and 1.68 (each 3H, s, (C$\underline{H}_3$)$_2$C=C), 1.7-2.1 (9H, m), 2.1-2.2 (1H, m), 2.25 (1H, dt, J=4, 14 Hz, HOCHC$\underline{H}_2$), 2.9-3.1 (1H, m, C$\underline{H}$C=C$\underline{H}_2$), 3.74 (1H, d, J=4 Hz, C$\underline{H}$OH), 4.75 and 4.84 (each 1H, s, C$\underline{H}_2$=C), 5.11 (1H, t, J=7 Hz, C$\underline{H}$=C). MS m/z: 288 (M^+). HRMS m/z: Calcd for $C_{20}H_{32}O$ (M^+): 288.24450. Found 288.2449.

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19) Cache system was used for MM and MOPAC calculations on Macintosh supported by IBM workstation. Organic extract was dried over $MgSO_4$. Silica gel chromatography was used. Melting points were measured using Büchi 510 melting point apparatus and are not corrected. Optical rotations were taken with a JASCO DIP-181 automatic polarimeter. Infra red spectra were taken with a JASCO Infrared spectrometer Model DS-402G and a JASCO IRA-I Grating Infrared Spectrometer. Proton nuclear magnetic resonance spectra were taken with a JEOL FX-100 Spectrometer at 100 MHz, or with a Hitachi R-24B Spectrometer at 60 MHz. $CDCl_3$ was used as a solvent unless otherwise noted. Chemical shifts are expressed in ppm relative to internal tetramethylsilane. Abbreviations are as follows: s, singlet; t, triplet; q, quartet; m, multiplet; br, broad. Mass spectra were taken with a JEOL JMS DX-300 MS spectrometer.

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