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Total Synthesis of Natural (+)-Spatol. Confirmation of The Absolute Stereostructure[1]

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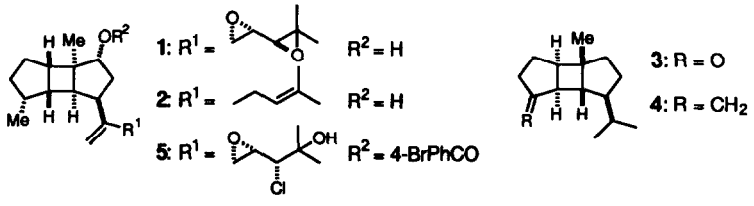
Abstract: *Total synthesis of optically pure spatol (+)-1 was achieved by employing asymmetric (2+2) photocycloaddition of the optically pure butenolide 12 with cyclopentenone ethylene ketal. The two major photocycloadducts 14, 15 were separately converted into the cis,anti,cis-tricyclo-[5.3.0.0^{2,6}]decane 9 and then to the sulfonium 11. Coupling of 11 through ylide with optically active epoxyaldehyde 24 provided optically pure 1 with definite absolute configuration.*

(+)-Spatol **1** is a representative of spatane diterpenes isolated from brown algae of south pacific ocean.[2] Spatane diterpenes are characterized by unique tricyclo[5.3.0.0^{2,6}]decane ring,[3] which is also found in bourbonene sesquiterpenes **3**, **4**[4] with the opposite absolute configuration. Furthermore, the tricyclic ring of spatol is attached by a vinyl diepoxide carbon chain with three contiguous chiral centers.[5]



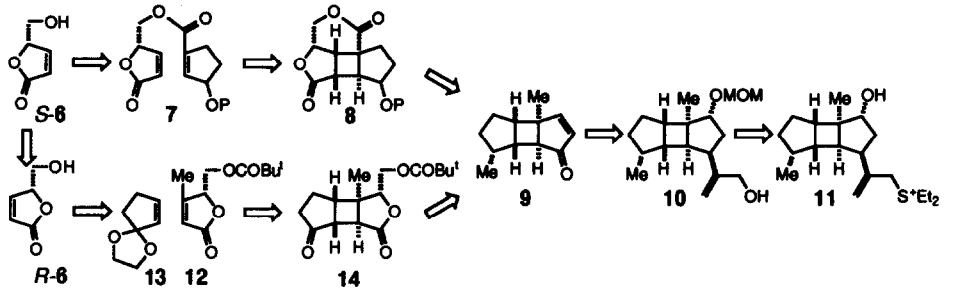
The stereochemistry of **1** was elucidated based on the X-ray crystallography of its bromobenzoate derivative **5**, in which one of the two epoxide rings was opened by chloride anion during derivatization.[2] However, the corresponding configuration was tentatively assigned to *S* assuming S_N2 opening of the epoxide with chloride anion to **5**. Along with these intriguing structural features, the potent cytotoxicity and limited supply from the natural source attracted much concern of synthetic chemists.[6]

We have already succeeded in the total synthesis of optically pure (+)-stoechospermol **2**, another representative of spatane diterpenes,[7] and bourbonene sesquiterpenes **3**, **4**[8] utilizing intramolecular and intermolecular asymmetric (2+2) photocycloadditions. In these syntheses, *cis,anti,cis*-tricyclo[5.3.0.0^{2,6}]-decane skeleton was constructed in both configurations starting from (*S*)-γ-hydroxymethyl-γ-butenolide **6**[9] by the application of the intramolecular or intermolecular mode of the photocycloaddition. Encouraged by these successful approaches, we focused our efforts on the total synthesis of optically pure spatol **1**, which is a subject of the present full article.[10]

Synthetic Strategy

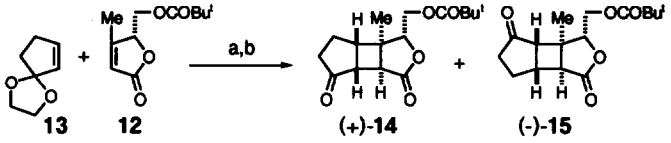
The synthesis of spatol **1** was essentially based on the same strategy applied for **2**.[7] Asymmetric (2+2) photocycloaddition of **7** or **12** provides optically pure *cis,anti,cis*-tricyclo[5.3.0.0^{2,6}]decane **9**, which is

convertible to an allylic alcohol **10** according to the already developed procedure.[7] Then, the allylic alcohol **10** is converted to the corresponding sulfonium **11**.[11] Coupling of **11** *through* sulfonium ylide with an optically active epoxy aldehyde with definite absolute configuration[12] would provide optically pure spatol **1** with definite absolute configuration.



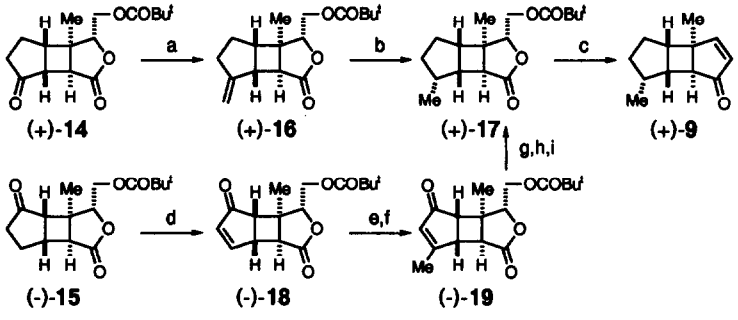
Preparation of the Key Intermediate 9

The intramolecular photocycloaddition approach is highly stereoselective, however, requires somewhat long route to reach **9**.[7] For the synthesis of **1**, we adapted the intermolecular photocycloaddition approach. The starting butenolide (*R*)-**6**, prepared from readily available (*S*)-**6** by the inversion of configuration,[13] was converted to (+)-**12** according to the previously developed procedure.[14] The key (2+2) photocycloaddition of (+)-**12** with **13** was conducted in acetonitrile under irradiation with low pressure mercury lamp to provide the four regio- and stereoisomeric photoadducts.[7] Acidic hydrolysis of these photoadducts followed by careful separation afforded the desired tricyclic ketones, (+)-**14** and (-)-**15** in 14% and 28% yield, respectively. The minor and undesired two stereoisomers were also isolated in 9% and 11% yields.[7]



a) hν (254nm), CH_3CN; b) 10%H_2SO_4, acetone **14**: 28%, **15**: 14%

Wittig olefination of **14** followed by stereoselective hydrogenation afforded **17** in 60% yield, which was then converted to **9** in four steps (i. MeLi, ii. LiOMe, iii. $NaIO_4$, iv. NaOH) in 76% overall yield.[7]



a) CH_3PPh_3Br, n-BuLi, DME, 60%; b) H_2, 10%Pd-C, AcOH, quant; c) MeLi, THF; LiOMe, MeOH-THF; $NaIO_4$ aq. AcOEt; NaOH, aq. MeOH, 76%; d) PhSeCl, AcOEt; H_2O_2, pyridine-CH_2Cl_2, 69%; e) CH_2N_2, THF; f) toluene, heat, 75%; g) H_2, 10% Pd-C, AcOEt, 93%; h) ethanedithiol, BF_3OEt_2, CH_2Cl_2, 92%; i) Raney Ni (W-4), EtOH, 95%

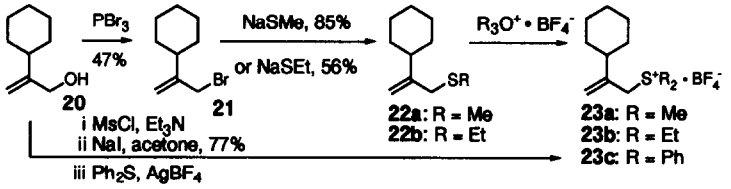
The conversion of **15** into **9** was achieved through **17**. Phenylselenylation and oxidation[15] of **15** provided **18**, which was then treated with diazomethane and heated in toluene to give **19**. Then, stereo-

selective hydrogenation of **19**, and deoxygenation *via* thioacetal provided **17**, which was identical with that obtained from **14**.

The optically pure key intermediate **9** was then converted into **10** by the procedure developed before.[7]

Model Study of the Vinylic Diepoxide Synthesis

Since the synthetic methodologies for linear and contiguous vinylic diepoxide systems are quite few,[5] we investigated model reaction of three sulfonium salts **23** with racemic epoxyaldehyde **24**. The sulfonium salts were prepared from **20**[16] as shown.



Treatment of **23a** with LDA or BuLi in DME followed by **24**, however, resulted in the formation of **28a** as a major product by preferential deprotonation at the methylthio group and following [2,3]-sigmatropic rearrangement. Attempted reaction by diphenyl sulfonium salt **23c** was also unsatisfactory to give rise to a mixture of diepoxides in low yield as shown in the Table 1. Fortunately, it was found that, when the diethyl sulfonium salt **23b** was treated with methyllithium as a base in the presence of 1 eq. of HMPA in DME followed by **24**, the desired vinylic diepoxide **25** was obtained as a major product in 25% yield among the possible other three isomers **26** and **27** (a mixture of 5:1 *trans* isomers) and **28b**.

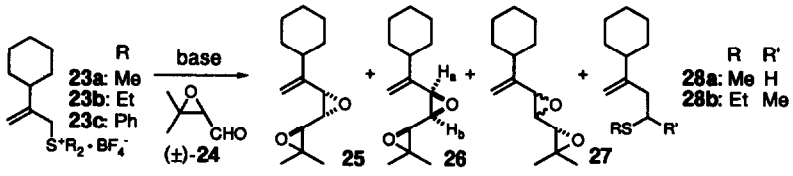
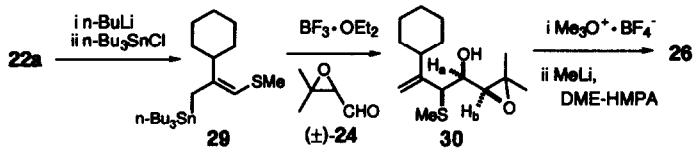


Table 1. Coupling of **23** with **24**

entry	23	R	Base	25/%	26/%	27[a]/%	28/%
1	**23a**	Me	LDA	0	0	0	74[b]
2			n-BuLi	4	0	5	40[b]
3	**23c**	Ph	LDA	3	0	2	-
4			n-BuLi	3	2	4	-
5	**23b**	Et	n-BuLi	11	5	17	19[c]
6			MeLi	20	5	19	7[c]
7			MeLi + HMPA (1 eq)	25	4	22	11[c]

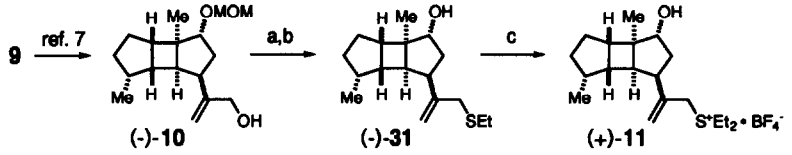
a) A mixture of 5:1 two *trans*-diastereomers. b) R'=H. c) R'=Me.

The structure of **25** was assigned based on the following experiments. The syn, syn-alcohol **30** ($J_{Ha\text{-}Hb}$ = 8 Hz),[17] prepared by coupling of allyl stannane **29** with **24** according to the established chemistry of Yamamoto and Keck,[18] was treated with $Me_3O^+ \cdot BF_4^-$ in dichloromethane and then with methyllithium in DME-HMPA to afford a *cis*-diepoxide **26** ($J_{Ha\text{-}Hb}$ = 4 Hz)[19] having the undesired relative configuration. Coupling constant between the protons of the newly created epoxide of **25** is 5 Hz and this indicates that **25** has the desired relative configuration identical with that of **1**.



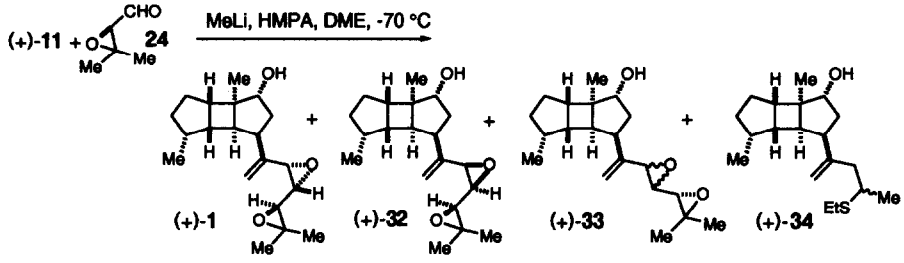
Total Synthesis of Optically Pure Spatol

The allylic alcohol **10** was converted to the crystalline sulfonium salt **11** in 79% overall yield in four steps (i. MsCl-Et_3N/CH_2Cl_2; ii. NaSEt/DMF; iii. 10% H_2SO_4/acetone; iv. $Et_3O{\cdot}BF_4/CH_2Cl_2$). The optically active epoxyaldehyde (*R*)-**24** was prepared from the corresponding known (*S*)-epoxyalcohol[12] by the Collins oxidation.



a) MsCl, Et_3N, CH_2Cl_2; EtSNa, DMF, 89%; b) 10%H_2SO_4 acetone, 92%; c) $Et_3O{\cdot}BF_4$ CH_2Cl_2, 75%

Treatment of **11** with methyllithium in the presence of 1 eq. of HMPA in DME at -70 °C for 1h and then with optically active (*R*)-**24** at -70 °C for 1h and then at rt for 1 h afforded, after careful separation by HPLC (Waters Radial Pak B, acetone-hexane/1:6), (+)-spatol **1** and two isomers **32**, **33**[20] in a ratio of 24:12:64 in 13% yield and the rearranged product **34** in 35% yield.



Optical rotation, melting point, tlc behavior, and spectroscopic data of the synthetic spatol **1** ($[\alpha]_D^{23}$ +45.5 °($CHCl_3$), mp 100-101 °C, mmp 100-102°C) were completely identical with those of the natural spatol ($[\alpha]_D$ +45.6 °($CHCl_3$), mp 100-102 °C), kindly provided by Dr. Fenical.[2] Since the optically pure epoxy aldehyde **24** with the definite absolute configuration was incorporated in **1**, the stereochemistry of natural spatol was firmly established.

Conclusion

The first total synthesis of (+)-spatol **1** with natural configuration was achieved by utilizing the intermolecular (2+2) photocycloaddition reaction for the construction of tricyclic skeleton and the reaction of sulfonium ylide with optically active epoxy aldehyde for the vinylic diepoxide moiety. The synthesis also served the direct evidence for the terminal epoxide stereochemistry to be *S*-configuration in natural spatol.

Experimental[21]

(+)-3-Methyl-4-pivaloyloxymethyl-2-methyl-2-buten-4-olide 12 Based on the reported procedure,[13,14] **12** was prepared as colorless needles of mp 64-66 °C (AcOEt-hexane). $[\alpha]_D^{20}$ +68.9°(c 1.05, $CHCl_3$).

Photocycloaddition of (+)-12 with 13 According to the procedure described before, a mixture of (+) **12** (3.95 g, 18 mmol) and **13** (18 mL, 0.16 mol) was irradiated by low pressure mercury lamp, and the products were separated. The first fraction contained diastereomeric ketal of **14** (1.6 g) as colorless oil. Purification was achieved by converting into the ketone. The second fraction contained diastereomeric ketal of **15** (0.62 g, 10%) as colorless needles of mp 114.5-115 °C (AcOEt-hexane). $[\alpha]_D^{20}$ -92.7 °(c 0.43, $CHCl_3$). Spectroscopic data were identical with those of its enantiomer.[7] The third fraction contained ketals of **15** and **14** as a colorless oil (4.3 g). Crystallization from AcOEt-hexane gave ketal of **14** as colorless needles (1.40 g, 22%) of mp 126-128 °C. $[\alpha]_D^{20}$ +22.9 °(c 0.35, $CHCl_3$). Spectroscopic data were identical with those of enantiomer. Separation of ketals of **15** and **14**, contained in mother liquor (1.85 g), was achieved by converting into ketones as described below.

(+)-(1*S*,2*R*,5*R*,6*S*,7*R*)-6-Methyl-5-pivaloyloxymethyl-4-oxatricyclo[5.3.0.0^{2,6}]decan-3,8-dione A solution of diastereomeric ketal of **14** (1.60 g, see above) and 10% H_2SO_4 (1.5 mL) in acetone (15 mL) was heated under reflux for 1 h. After neutralization with satd. $NaHCO_3$, the mixture was extracted with CH_2Cl_2 (20 mL x 3), and the combined extracts were dried. Concentration and column chromatography (AcOEt-hexane 1:2) afforded colorless needles of mp 83.5-84.5 °C (AcOEt-hexane) (0.61 g, 11% form (+)-**12**). $[\alpha]_D^{20}$ +37.4 °(c 0.93, $CHCl_3$). IR (KBr): 1775, 1720 cm^{-1}. NMR δ: 1.24 (9H, s, ($C\underline{H}_3$)$_3$), 1.28 (3H, s, $C\underline{H}_3$), 1.9-2.6 (4H, m, ($C\underline{H}_2$)$_2$), 2.7-3.1 (3H, m, C$\underline{H}$), 4.2-4.5 (3H, m, OC$\underline{H}_2$C$\underline{H}$O). MS m/z: 295 (M^++1). Anal. Calcd for $C_{16}H_{22}O_5$: C, 65.29; H, 7.53. Found: C, 65.03; H, 7.39.

(+)-(1*R*,2*S*,5*R*,6*R*,7*S*)-6-Methyl-5-pivaloyloxymethyl-4-oxatricyclo[5.3.0.0^{2,6}]decan-3,10-dione 14 and (-)-(1*R*,2*S*,5*R*,6*R*,7*S*)-6-methyl-5-pivaloyloxymethyl-4-oxatricyclo[5.3.0.0^{2,6}]-decan-3,8-dione 15 A mixture containing ketals of **15** and **14** (1.85 g, obtained from the above mother liquor) and 10% H_2SO_4 (10 mL) in acetone (50 mL) was heated under reflux for 1h. After neutralization with satd. $NaHCO_3$, the mixture was concentrated, taken up into CH_2Cl_2 (50 mL), washed with water, and dried. Concentration and column chromatography (AcOEt-hexane 1:2) afforded (+)-**14** (0.35 g, 6% form (+)-**12**) as colorless needles of mp 132-133 °C (AcOEt-hexane) and (-)-**15** (0.76 g, 14% from (+)-**12**) as colorless plates of mp 110-112 °C (AcOEt-hexane). (+)-**14**: $[\alpha]_D^{20}$ +154 °(c 0.96, $CHCl_3$). IR (KBr): 1775, 1740 cm^{-1}. NMR δ: 1.17 (9H, s, ($C\underline{H}_3$)$_3$), 1.20 (3H, s, $C\underline{H}_3$), 1.9-2.3 (2H, m), 2.3-2.7 (2H, m), 2.7-2.8, 2.8-2.9, 3.0-3.2 (each 1H, m), 4.04, 4.36 (each 1H, dd, J=2, 12 Hz, OC$\underline{H}_2$CHO), 4.55 (1H, t, J=2 Hz, C$\underline{H}$). MS m/z: 295 (M^++1). Anal. Calcd for $C_{16}H_{22}O_5$: C, 65.29; H, 7.53. Found: c, 65.50; H, 7.66. (-)-**15**: $[\alpha]_D^{20}$ -121 °(c 1.09, $CHCl_3$). IR (KBr): 1775, 1725 cm^{-1}. NMR δ: 1.18 (9H, s, ($C\underline{H}_3$)$_3$), 1.24 (3H, s, $C\underline{H}_3$), 2.0-2.6 (4H, m, ($C\underline{H}_2$)$_2$), 2.6-3.1 (3H, m, C$\underline{H}$C$\underline{H}$C$\underline{H}$), 4.06, 4.36 (1H, dd, J=3, 14 Hz, OC$\underline{H}_2$CH), 4.65 (1H, t, J=3 Hz, C$\underline{H}$). MS m/z 294 (M^+). Anal. Calcd for $C_{16}H_{22}O_5$: C, 65.29; H, 7.53. Found: C, 65.14; H, 7.53.

(+)-(1*R*,2*S*,5*R*,6*R*,7*S*)-6-Methyl-5-pivaloyloxymethyl-4-oxatricyclo[5.3.0.0^{2,6}]decan-3,10-dione 14 A mixture of above crude ketal (1.40 g) and 10% H_2SO_4 (1.7 mL) in acetone (27 mL) was refluxed for 1 h. Work up as described above afforded (+)-**14** as colorless needles (1.22 g, quant).

(-)-(1*S*,2*R*,5*R*,6*S*,7*R*)-6-Methyl-5-pivaloyloxymethyl-4-oxatricyclo[5.3.0.0^{2,6}]decan-3,10-dione Similarly, the compound was prepared from the above ketal as colorless needles (93%) of mp 161-163 °C (AcOEt-hexane). $[\alpha]_D^{20}$ -218 °(c 0.93, $CHCl_3$). IR (KBr): 1780, 1730 cm^{-1}. NMR δ: 1.24 (9H, s, ($C\underline{H}_3$)$_3$), 1.31 (3H, s, $C\underline{H}_3$), 1.8-2.2, 2.2-2.6, 2.7-2.9 (each 2H, m), 3.1-3.3 (1H, m), 4.34 (3H, s, OC$\underline{H}_2$C$\underline{H}$O). MS m/z: 294 (M^+). Anal. Calcd for $C_{16}H_{22}O_5$: C, 65.29; H, 7.53. Found: c, 65.02; H, 7.58.

(+)-(1*R*,2*S*,5*R*,6*R*,7*S*)-6-Methyl-10-methylene-5-pivaloyloxymethyl-4-oxatricyclo-[5.3.0.0^{2,6}]decan-3-one 16 *n*-BuLi (1.50 M in hexane, 0.22 mL, 0.33 mmol) was added to a suspension of methyltriphenylphosphonium bromide (121 mg, 0.34 mmol) in DME (1.5 mL) at 0 °C, and the mixture was stirred at 0 °C for 1 h. Then the supernatant (1.3 mL, 0.25 mmol) was added to a solution of (+)-**14** (50 mg, 0.17 mmol) in DME (4.5 mL) at -10 °C. The whole was stirred at rt for 1 h, and a mixture of satd NH_4Cl and satd. NaCl was added. After extraction with CH_2Cl_2 (10 mL x 3), the combined extracts were washed with satd. NaCl, and dried. Concentration and column chromatography (ether-benzene 1:20) afforded (+)-**16** (30 mg, 60%) as a colorless oil. $[\alpha]_D^{23}$ +79.4 °(c 1.14, $CHCl_3$). IR (neat): 1775, 1735 cm^{-1}. NMR δ: 1.16 (3H, s, $C\underline{H}_3$), 1.18 (9H, s, ($C\underline{H}_3$)$_3$), 1.7-2.0 (2H, m), 2.4-2.7 (3H, m), 2.8-3.0, 3.1-3.3 (each 1H, m), 4.06, 4.34 (each 1H, dd, J=3, 12 Hz, OC$\underline{H}_2$CH), 4.56 (1H, t, J=3 Hz, C$\underline{H}$O), 5.0-5.1 (2H, m, C=C$\underline{H}_2$). MS m/z: 292 (M^+). HRMS m/z: Calcd for $C_{17}H_{24}O_4$ (M^+): 292.1674. Found: 292.1676.

(+)-(1*R*,2*S*,5*R*,6*R*,7*S*,10*R*)-6,10-Dimethyl-5-pivaloyloxymethyl-4-oxatricyclo[5.3.0.0^{2,6}]-decan-3-one 17 A solution of (+)-**16** (1.40 g) and acetic acid (5 mL) in EtOH (50 mL) was hydrogenated over 10% Pd-C (0.2 g) under H_2 at rt for 22 h. After filtration, the filtrate was neutralized with satd. $NaHCO_3$, concentrated, and extracted with CH_2Cl_2 (50 mL x 3). The extract was dried. Concentration afforded (+)-**17** (1.40 g, quant.) as a colorless oil. $[\alpha]_D^{24}$ +1.53 °(c 1.05, $CHCl_3$). IR (neat): 1775, 1730 cm^{-1}. NMR δ: 1.03 (3H, s, C<u>H</u>$_3$), 1.06 (3H, d, J=7 Hz, C<u>H</u>$_3$), 1.20 (9H, s, (C<u>H</u>$_3$)$_3$), 1.5-2.2 (5H, m), 2.45 (1H, d, J=5 Hz, C<u>H</u>CO), 2.62 (1H, t, J=7 Hz, CH$_2$C<u>H</u>), 2.82 (1H, dd, J=5, 7 Hz, C<u>H</u>CH), 4.12 (1H, dd, J=6, 12 Hz, OC<u>H</u>$_2$CH), 4.34 (1H, dd, J=4, 12 Hz, OC<u>H</u>$_2$CH), 4.70 (1H, dd, J=4, 6 Hz, C<u>H</u>OCO). MS m/z: 294 (M$^+$). HRMS m/z: Calcd for $C_{17}H_{26}O_4$ (M$^+$): 294.1831. Found: 294.1856.

(+)-(1*R*,2*S*,6*S*,7*S*,10*R*)-10,6-Dimethyltricyclo[5.3.0.0^{2,6}]dec-4-en-3-one 9 MeLi (1.40 M in ether, 4.5 mL, 6.3 mmol) was added to a solution of (+)-**17** (1.42 g, 4.8 mmol) in THF (35 mL) at -78 °C, and the mixture was stirred at -78 °C for 20 min, and MeOH (10 mL) was added. The whole was heated under reflux for 1 h. After concentration , water (15 mL) and AcOEt (30 mL) were added, and the mixture was stirred at rt for 30 min. Then $NaIO_4$ (3.0 g, 14 mmol) was added, and the mixture was stirred at rt for 2 h. After extraction with AcOEt (15 mL x 2), the combined extracts were washed with water, satd. $Na_2S_2O_3$, and satd. NaCl, then dried. Concentration afforded the ketoaldehyde (1.0 g) as a colorless oil. A solution of ketoaldehyde (1.05 g) in MeOH (22 mL) and 15% NaOH (8.6 mL) was stirred at rt for 1 h, and water (50 mL) was added. After extraction with CH_2Cl_2 (20 mL x 3), the combined extracts were dried. Concentration and column chromatography (AcOEt-hexane 1:10) afforded (+)-**9** (0.65 g, 76%) as a colorless oil. $[\alpha]_D^{23}$ +214 °(c 1.78, $CHCl_3$). IR (neat): 1700, 1580 cm^{-1}. NMR δ: 1.06 (3H, s, C<u>H</u>$_3$), 1.07 (3H, d, J=7 Hz, C<u>H</u>$_3$), 1.2-2.6 (8H, m), 6.16, 7.51 (each 1H, d, J=7 Hz, C<u>H</u>=CH). MS m/z: 176 (M$^+$). HRMS m/z: Calcd for $C_{12}H_{16}O$ (M$^+$): 176.1199. Found: 176.1186.

(-)-(1*R*,2*S*,5*R*,6*R*,7*S*)-6-Methyl-5-pivaloyloxymethyl-4-oxatricyclo[5.3.0.0^{2,6}]dec-9-ene-3,8-dione 18 A solution of (-)-**15** (2.66 g, 9.05 mmol) and phenylselenyl chloride (2.80 g, 14.6 mmol) in AcOEt (50 mL) was stirred at rt for 1.5 h and concentrated. To a solution of the residue and pyridine (6 mL) in CH_2Cl_2 (100 mL) was added 15% H_2O_2 (3.6 mL, 16 mmol) at 0 °C, and the whole was stirred at 0 °C for 1.5 h, washed with water, satd. $Na_2S_2O_3$, water, 10% HCl, water, and satd. $NaHCO_3$, then dried. Concentration and chromatography (ether-benzene 1:3) afforded (-)-**18** (1.77 g, 69%) as colorless needles of mp 125-126 °C (AcOEt-hexane). $[\alpha]_D^{24}$ -208 °C (c 0.42, $CHCl_3$). IR (KBr): 1770, 1730, 1690 cm^{-1}. NMR δ: 1.17 (9H, s, (C<u>H</u>$_3$)$_3$), 1.18 (3H, s, C<u>H</u>$_3$), 2.74 (1H, d, J=1 Hz, C<u>H</u>), 3.12 (1H, d, J=5 Hz, C<u>H</u>COO), 3.5-3.6 (1H, m), 4.06 (1H, dd, J=2, 12 Hz, OC<u>H</u>$_2$CH), 4.39 (1H, dd, J=3, 12 Hz, OC<u>H</u>$_2$CH), 4.76 (1H, dd, J=2, 3 Hz, C<u>H</u>OCO), 6.49 (1H, dd, J=1, 5 Hz, CH=C<u>H</u>CO), 7.87 (1H, dd, J=3, 5 Hz, C<u>H</u>=CH). MS m/z 292 (M$^+$). Anal. Calcd for $C_{16}H_{20}O_5 \cdot 1/4H_2O$: C, 64.74; H, 6.96. Found: C, 64.83; H, 6.85.

(-)-(1*R*,2*S*,5*R*,6*R*,7*S*)-6,10-Dimethyl-5-pivaloyloxymethyl-4-oxatricyclo[5.3.0.0^{2,6}]dec-9-ene-3,8-dione 19 *N*-Methyl-*N*-nitrosourea (12 g) was added to a mixture of ether (70 mL) and 40% KOH (35 mL) at 0 °C. Ether layer was added to a solution of (-)-**18** (1.77 g, 6.06 mmol) in THF (35 mL). The whole was stirred at 0 °C for 3 h, and concentrated. A solution of the residue in toluene (100 mL) was heated under reflux for 1 h. Concentration and column chromatography (AcOEt-hexane 1:5) afforded (-)-**19** (1.40 g, 75%) as colorless needles of mp 165-166 °C (AcOEt-hexane). $[\alpha]_D^{24}$ -162 °(c 0.87, $CHCl_3$). IR (KBr): 1770, 1740, 1690 cm^{-1}. NMR δ: 1.18 (12H, s, (C<u>H</u>$_3$)$_3$ and C<u>H</u>$_3$), 2.25 (3H, s, C<u>H</u>$_3$C=C), 2.63 (1H, d, J=2 Hz, C<u>H</u>), 3.13 (1H, d, J=5 Hz, C<u>H</u>COO), 3.31 (1H, dd, J=2, 5 Hz, C<u>H</u>CHCO), 4.05 and 4.40 (each 1H, dd, J=12, 3 Hz, OC<u>H</u>$_2$CH), 4.75 (1H, t, J=3 Hz, C<u>H</u>OCO), 6.22 (1H, br, C=C<u>H</u>CO). MS m/z: 306 (M$^+$). Anal. Calcd for $C_{17}H_{22}O_5$: C, 66.65; H, 7.24. Found: C, 66.41; H, 7.30.

(-)-(1*R*,2*S*,5*R*,6*R*,7*S*,10*R*)-6,10-Dimethyl-5-pivaloyloxymethyl-4-oxatricyclo[5.3.0.0^{2,6}]-decan-3,8-dione A solution of (-)-**19** (1.40 g) in AcOEt (30 mL) was hydrogenated over 10% Pd-C (100 mg) under H_2 at rt for 24 h. After filtration, the filtrate was concentrated to give colorless plates of mp 123-124 °C (AcOEt-hexane) (1.31 g, 93%). $[\alpha]_D^{25}$ -177 °(c 1.08, $CHCl_3$). IR (KBr): 1780, 1730 cm^{-1}. NMR δ: 1.10 (3H, s, C<u>H</u>$_3$), 1.21 (9H, s, (C<u>H</u>$_3$)$_3$), 1.22 (3H, d, J= 6 Hz, C<u>H</u>$_3$), 2.1-2.9 (5H, m), 3.0-3.2 (1H, m), 4.17 (1H, dd, J=12, 6 Hz, OC<u>H</u>$_2$CH), 4.36 (1H, dd, J=12, 4 Hz, C<u>H</u>$_2$CH), 4.75 (1H, dd, J=4, 6 Hz, C<u>H</u>OCO). MS m/z: 309 (M$^+$+1). Anal. Calcd for $C_{17}H_{24}O_5$: C, 66.21; H, 7.85. Found: C, 65.95; H, 7.88.

(+)-(1*S*,2*S*,5*R*,6*S*,7*S*,10*R*)-8-Ethylenedithio-6,10-dimethyl-5-pivaloyloxymethyl-4-oxatricyclo[5.3.0.0^{2,6}]decan-3-one A solution of **19** (1.31 g, 4.3 mmol), ethanedithiol (2.5 mL, 30 mmol) and BF_3OEt_2 (0.2 mL) in CH_2Cl_2(50 mL) was stirred at rt for 2 days, then washed with water and satd. $NaHCO_3$, and dried. Concentration and chromatography (AcOEt-hexane 1:5) afforded colorless needles of mp 112.5-113 °C (AcOEt-hexane) (1.50 g, 92%). $[\alpha]_D^{24}$ +16.7 °(c 1.22, $CHCl_3$). IR (KBr): 1775, 1730 cm^{-1}. NMR δ: 1.11 (3H, d, J= 7 Hz, C$\underline{H}_3$), 1.20 (9H, s, (C$\underline{H}_3$)$_3$), 1.33 (3H, s, C$\underline{H}_3$), 2.0-2.7 (4H, m), 2.8-3.0 (2H, m), 3.1-3.4 (4H, m, S(C$\underline{H}_2$)$_2$S), 4.14, 4.35 (each 1H, dd, J=12, 4 Hz, OC$\underline{H}_2$CH), 4.68 (1H, t, J=4 Hz, C$\underline{H}$). MS m/z: 384 (M$^+$). Anal. Calcd for $C_{19}H_{28}O_4S_2$: C, 59.34; H, 7.34. Found: C, 59.19; H, 7.34.

(+)-(1*R*,2*S*,5*R*,6*R*,7*S*,10*R*)-6,10-Dimethyl-5-pivaloyloxymethyl-4-oxatricyclo[5.3.0.0^{2,6}]-decan-3-one 17 A suspension of above dithioacetal (1.45 g), Raney Ni (W-4) (10 mL) in EtOH (100 mL) was heated under reflux for 2 h. Nickel was filtered off, and the filtrate was concentrated and purified by column chromatography (AcOEt-hexane 1:5) to afford (+)-**17** (1.05 g, 95%) as a colorless oil. $[\alpha]_D^{24}$ +1.56 °(c 0.90, $CHCl_3$). Spectroscopic data were identical in all respects with those of (+)-**17** prepared from **16**.

2-Cyclohexyl-1-bromoprop-2-ene 21 Phosphorous tribromide (0.55 mL, 8.3 mmol) was added to a solution of **20** (1.40 g, 10 mmol) in ether (10 mL) at 0 °C and the mixture was stirred at 0 °C for 1.5 h. The mixture was washed with satd. $NaHCO_3$, water, and satd NaCl, then dried. Concentration afforded **21** as a colorless oil (0.95 g, 47%). IR (neat): 3100, 2950, 2850, 1640 cm^{-1}. NMR δ: 0.8-2.5 (11H, m), 3.95 (2H, s, C$\underline{H}_2$Br), 4.90 and 5.07 (each 1H, s, C=C$\underline{H}_2$). MS m/z: 202 (M$^+$) 123 (M$^+$-Br).

2-Cyclohexyl-1-methylthioprop-2-ene 22a A 15% solution of sodium thiomethoxide in water (5 mL, 11 mmol) was added to a solution of **21** (0.94 g, 4.6 mmol) in ethanol (10 mL). The mixture was stirred at rt of 4.5 h, and taken up into ether, washed with satd. NaCl, and dried. Concentration and distillation afforded **22a** as a colorless oil (0.79 g, 85%) of bp 150 °C/12 mmHg. IR (neat): 3100, 1640 cm^{-1}. NMR δ: 1.0-2.8 (11H, m), 1.95 (3H, s, SC$\underline{H}_3$), 3.10 (2H, s, C$\underline{H}_2$S), 4.80 (2H, s, C=C$\underline{H}_2$). MS m/z: 170 (M$^+$).

2-Cyclohexyl-1-ethylthioprop-2-ene 22b Ethanethiol (0.88 mL, 12 mmol) was added to a solution of sodium ethoxide in EtOH (10 mL, 12.5 mmol) followed by a solution of **21** (2.4 g, 12 mmol) in EtOH (5 mL). The mixture was stirred at rt for 1 h, taken up into ether, and washed with satd. NaCl, then dried. Concentration and distillation afforded **22b** as a colorless liquid (1.22 g, 56%) of bp. 130 °C/5 mmHg. IR (neat): 3100, 2950, 2850, 1635 cm^{-1}. NMR δ: 0.8-2.5 (11H, m), 1.22 (3H, t, J=7 Hz, C$\underline{H}_3$), 2.45 (2H, q, J=7 Hz, C$\underline{H}_2$), 3.18 (2H, s, C$\underline{H}_2$S), 4.84 (2H, s, C=C$\underline{H}_2$). MS m/z: 184 (M$^+$).

Preparation of sulfonium salt 23b, generation of ylide, and coupling with 24 (Table, entry 5) $Et_3O{\cdot}BF_4$ (99 mg, 0.52 mmol) was added to a solution of **22b** (85 mg, 0.46 mmol) in CH_2Cl_2 (2 mL) and the mixture was stirred at rt for 3 h. After concentration, the residual sulfonium salt (**23b**) was dissolved in DME (3 mL) and cooled to -78 °C. After addition of *n*-BuLi (1.50 M in hexane, 0.36 mL, 0.50 mmol), the mixture was stirred for 10 min. A solution of (±)-**24** (20% in ether, 0.3 mL, 0.6 mmol) in DME (1 mL) was added at -78 °C, and the mixture was stirred at -78 °C for 1 h and at rt for 1 h. After addition of water, the mixture was extracted with ether (30 mL). The combined extracts were dried. Concentration and chromatography (AcOEt-hexane 1:50) gave a 1:1 mixture of **25** and one isomer of **27** as a colorless oil (22 mg, 22%), **26** as a colorless oil (5 mg, 5%), another isomer of **27** as a colorless oil (6 mg, 6%), and **28b** as a colorless oil (19 mg, 19%). **25** and one isomer of **27**: IR (neat): 3100, 2950, 1640 cm^{-1}. NMR δ: 0.9-2.1 (17H, m), 2.52 (0.5H, d, J=8 Hz, C$\underline{H}$(O)CMe$_2$ of **25**), 2.61 (0.5H, d, J=6 Hz, C$\underline{H}$(O)CMe$_2$ of **27**), 2.67 (0.5H, dd, J=2, 6 Hz, C=CCH(O)C$\underline{H}$ of **27**), 2.90 (0.5H, d, J=5, 8 Hz, C=CCH(O)C$\underline{H}$ of **25**), 3.36 (0.5H, dd, J=2, 1 Hz, C=CC$\underline{H}$(O)CH of **27**), 3.54 (0.5 H, d, J=5, 1 Hz, C=CC$\underline{H}$(O)CH of **25**), 4.88, 4.98 (each 0.5 H, s, C=C$\underline{H}_2$), 5.01 (1H, s, C=C$\underline{H}_2$). MS m/z: 233 (M$^+$+1), 207 (M$^+$-CH$_3$). **26**: IR (neat): 3100, 2950, 1650 cm^{-1}. NMR δ: 1.0-1.5 (5H, m), 1.28, 1.36 (each 3H, s, C$\underline{H}_3$), 1.6-2.1 (6H, m), 2.53 (1H, d, J=8 Hz, C$\underline{H}$(O)CMe$_2$), 2.85 (1H, dd, J=8, 5 Hz, CH(O)C$\underline{H}$), 3.48 (1H, dd, J=5, 1 Hz, C$\underline{H}$(O)CH), 4.96, 5.07 (each 1H, s, C=C$\underline{H}_2$). MS m/z: 222 (M$^+$). Another isomer of **27**: IR (neat): 2950 cm^{-1}. NMR δ: 1.0-1.5 (5H, m), 1.36, 1.41 (each 3H, s, C$\underline{H}_3$)), 1.6-2.0 (6H, m), 2.63 (1H, d, J=6 Hz C$\underline{H}$(O)CMe$_2$), 2.72 (1H, dd, J=2, 6 Hz, CH(O)C$\underline{H}$), 3.29 (1H, d, J=2 Hz, C$\underline{H}$(O)CH), 4.89, 5.04 (each 1H, s, C=C$\underline{H}_2$). MS m/z: 222 (M$^+$). **28b**: IR (neat): 3100, 1640 cm^{-1}. NMR δ: 1.0-1.4 (5H, m), 1.4-2.0 (6H, m), 1.24 (3H, t, J=7 Hz, C$\underline{H}_3$), 1.22 (3H, d, J=6 Hz, C$\underline{H}_3$), 2.10 (1H, dd, J=5, 9 Hz, C=CC$\underline{H}_2$), 2.44 (1H, dd, J=5, 13 Hz, C=CC$\underline{H}_2$), 2.7-3.0 (1H, m, SC$\underline{H}$), 2.58 (2H, q, J=7 Hz, SC$\underline{H}_2$), 4.6-4.9 (2H, m, C=C$\underline{H}_2$). MS m/z: 212 (M$^+$).

Preparation of sulfonium salt 23a, generation of ylide, and coupling with 24 (Table, entry 2) $Me_3O{\cdot}BF_4$ (62 mg, 0.42 mmol) was added to a solution of **22a** (65 mg, 0.38 mmol) in CH_2Cl_2 (2 mL) and the mixture was stirred at rt for 40 min. After concentration, the residual sulfonium salt (**23a**) was treated as described above affording a 1:1 mixture (**25** and one isomer of **27**) (7 mg, 8%), another isomer of **27** (0.7 mg, 1%), and **28a** as a colorless oil (40 mg, 40%). **28a**: IR (neat): 3100, 1640 cm^{-1}. NMR δ: 0.8-2.0 (11H, m), 2.10 (3H, s, SCH_3), 2.2-2.9 (4H, m), 4.6-4.8 (2H, m, $C{=}CH_2$). MS m/z: 184 (M^+).

Preparation of sulfonium salt 23c, generation of ylide, and coupling with 24 (Table, entry 4) A solution of **20** (1.15 g, 8.2 mmol), methanesulfonyl chloride (0.76 mL, 9.8 mmol), and triethylamine (1.6 mL, 10.8 mmol) in CH_2Cl_2 (20 mL) was stirred at 0 °C for 1.5 h, and then washed with 10% HCl, water, and satd. $NaHCO_3$, then dried. Concentration afforded mesylate of **20** (1.83 g, quant.) as a colorless oil. A solution of mesylate (0.50 g) and sodium iodide (0.66 g, 4.4 mmol) in acetone (5 mL) was stirred at rt for 1 h, taken up into ether, and the mixture was washed with 10% $Na_2S_2O_3$, water, and satd. NaCl, then dried. Concentration gave the corresponding iodide as a pale yellow oil (0.44 g, 77%). To a solution of iodide (99 mg, 0.40 mmol) and diphenyl sulfide (0.65 mL, 3.9 mmol) in nitromethane (1 mL) was added $AgBF_4$ (92 mg, 0.47 mmol), and the mixture was stirred at rt for 2.5 h. After addition of CH_2Cl_2 (5 mL), the mixture was filtered, concentrated, taken up into ether, and the supernatant was decanted off. The residue was dried under reduced pressure affording **23c** as a colorless oil (88 mg). Generation of ylide and following coupling afforded **26** (1 mg, 2%), and a 1:1 mixture of **25** and **27** (4 mg, 7%).

(3*S*,4*S*,5*S*)-2-Cyclohexyl-5,6-epoxy-4-hydroxy-6-methyl-3-methylthiohept-1,5-diene 30 *n*-BuLi (1.50 M in hexane, 0.74 mL, 1.1 mmol) was added to a solution of **22a** (170 mg, 1.0 mmol) and HMPA (0.35 mL, 2 mmol) in THF (8 mL) at -20 °C, and the mixture was stirred at -20 °C for 30 min. Tri-*n*-butyltin chloride (0.30 mL, 1.1 mmol) was added at -70 °C. The mixture was stirred at rt for 15 min and quenched with water. The mixture was extracted with ether. The extract was washed with water and brine, then dried. Concentration afforded **29** as a colorless oil (0.54 g). $BF_3{\cdot}OEt_2$ (0.05 mL, 0.42 mmol) was added to a solution of **29** (207 mg) and **24** (20% in ether, 0.36 mL, 0.72 mmol) in CH_2Cl_2 (4 mL) at -78 °C, stirred at -78 °C for 5 min, and quenched by satd. $NaHCO_3$. The mixture was extracted with ether. The extract was washed with satd. NaCl, and dried. Concentration and chromatography (ether-benzene 1:1) afforded **30** as a colorless oil (21 mg, 20% from **22a**). IR (neat): 3440, 1635 cm^{-1}. NMR δ: 0.8-2.0 (17H, m), 2.05 (3H, s, SCH_3), 2.62 (1H, d, J=3 Hz, OH), 2.81 (1H, d, J=8 Hz, SCH), 3.20 (1H, d, J=8 Hz, $CH(O)CMe_2$), 3.6) (1H, dt, J=3, 8 Hz, CHOH), 4.90, 5.05 (each 1H, s, $C{=}CH_2$). MS m/z: 270 (M^+).

Transformation of 30 to 26 A solution of **30** (6 mg, 0.022 mmol) and $Me_3O{\cdot}BF_4$ (4 mg, 0.027 mmol) in CH_2Cl_2 (0.5 mL) was stirred at rt for 2 h. After concentration, the residue was dissolved in DME (1 mL). HMPA (3.8 μL, 0.022 mmol) and MeLi (0.86 M in ether, 0.03 mL, 0.026 mmol) were added at -78 °C, and the mixture was stirred at -78 °C for 40 min and then at rt for 1.5 h, and quenched by pH 7 phosphate buffer, then extracted with CH_2Cl_2. The extract was dried. Concentration and column chromatography afforded **26** as a colorless oil (0.5 mg, 10%).

(-)-(1*S*,2*R*,3*R*,5*R*,6*R*,7*S*,8*R*)-5-(1-Ethylthio-2-propen-2-yl)-3-methoxymethoxy-2,8-dimethyltricyclo[5.3.0.0^{2,6}]decane A solution of (-)-**10** (311 mg, 1.11 mmol), methanesulfonyl chloride (0.16 mL, 2.1 mmol) and triethylamine (0.40 mL, 2.9 mmol) in CH_2Cl_2 (10 mL) was stirred at 0 °C for 30 min and diluted with CH_2Cl_2 (20 mL), then washed with 5% HCl, water, and satd. $NaHCO_3$, then dried. Concentration afforded mesylate of (-)-**10** (413 mg, quant.) as a colorless oil. Sodium thioethoxide (0.67 M in DMF, 1.7 mL, 1.2 mmol) was added to a solution of above mesylate (413 mg, 1.11 mmol) in DMF (3 mL) at 0 °C, and the whole was stirred at rt for 20 min, and diluted with benzene (50 mL), then washed with water and satd. NaCl, then dried. Concentration and chromatography (AcOEt-benzene 1:100) gave a colorless oil (319 mg, 89%). $[\alpha]_D^{24}$ -2.56°(c 0.86, $CHCl_3$). IR (neat): 3100, 1630 cm^{-1}. NMR δ: 0.88 (3H, d, J=7 Hz, CH_3), 1.00 (3H, s, CH_3), 1.1-1.5 (2H, m), 1.23 (3H, t, J=7 Hz, CH_3), 1.5-2.2 (7H, m), 2.2-2.7 (3H, m), 2.9-3.4 (3H, m), 3.36 (3H, s, OCH_3), 3.62 (1H, d, J=4 Hz, $CHOCH_2$), 4.56, 4.68 (each 1H, d, J=7 Hz, OCH_2O), 4.87 (1H, t, J=2 Hz, $CH_2{=}C$), 4.98 (1H, br, $CH_2{=}C$). MS m/z: 324 (M^+).

(-)-(1*S*,2*R*,3*R*,5*R*,6*R*,7*S*,8*R*)-5-(1-Ethylthio-2-propen-2-yl)-3-hydroxy-2,8-dimethyltricyclo-[5.3.0.0^{2,6}]decane 31 A solution of above sulfide (88 mg, 0.27 mmol) and 10% H_2SO_4 (0.5 mL) in acetone (5 mL) was heated under reflux for 2.5 h. After dilution with benzene (50 mL), the mixture was washed with satd. $NaHCO_3$ and satd. NaCl, then dried. Concentration and chromatography (AcOEt-benzene

1:10) gave (-)-**31** (70 mg, 92%) as colorless needles of mp 101-102.5 °C (hexane). $[\alpha]_D^{24}$ +49.6°(c 0.73, $CHCl_3$). IR (KBr): 3300, 1630 cm^{-1}. NMR δ: 0.88 (3H, d, J=8 Hz, CH_3), 1.00 (3H, s, CH_3), 1.0-2.1 (10H, m), 1.22 (3H, t, J=7 Hz, CH_3), 2.27 (1H, dt, J=4, 13 Hz, CH_2), 2.44 (2H, q, J=7 Hz, SCH_2), 2.96 and 3.16 (each 1H, d, J=14 Hz, $SCH_2C{=}CH_2$), 3.1-3.5 (1H, m), 3.75 (1H, d, J=4 Hz, HOCH), 4.87 (1H, t, J=2 Hz, $C{=}CH_2$), 4.98 (1H, t, J=1 Hz, $C{=}CH_2$). MS m/z: 280 (M^+): 280 (M^+). Anal. Calcd for $C_{17}H_{28}OS$: C, 72.80; H, 10.06. Found: C, 72.66; H, 10.20.

(+)-Diethyl 2-((1*S*,2*R*,3*R*,5*R*,6*R*,7*S*,10*R*)-5-hydroxy-6,10-dimethyltricyclo[5.3.0.0^{2,6}]decan-3-yl)prop-2-en-1-yl sulfonium tetrafluoroborate 11 A solution of (-)-**31** (9 mg, 0.032 mmol) and $Et_3O{\cdot}BF_4$ (6.7 mg, 0.035 mmol) in CH_2Cl_2 (0.5 mL) was stirred at rt for 70 h. After concentration, the residue was crystallized from ether to give (+)-**11** (9.6 mg, 75%) as colorless plates of mp 123-126 °C (CH_2Cl_2-ether). Concentration of the mother liquor afforded the recovered (-)-**31** (2 mg, 22% recovery). **11**: $[\alpha]_D^{24}$ +84.2 °(c 0.24, $CHCl_3$). IR (KBr): 3300, 1625 cm^{-1}. NMR δ: 0.89 (3H, d, J=5 Hz, CH_3), 1.02 (3H, s, CH_3), 1.1-2.1 (11H, m), 1.50, 1.53 (each 3H, t, J=7 Hz, $S(CH_2CH_3)_2$), 2.28 (1H, dt, J=4, 13 Hz, CH_2CH), 2.9-3.2 (1H, m, $CHC{=}CH_2$), 3.37 and 3.40 (each 1H, q, J=7 Hz, $S(CH_2CH_3)_2$), 3.48 (2H, q, J=7 Hz, $S(CH_2CH_3)_2$), 3.78 and 4.15 (each 1H, d, J=13 Hz, CH_2S), 3.80 (1H, d, J=5 Hz, HOCH), 5.35 (1H, d, J=2 Hz, $CH_2{=}C$), 5.58 (1H, s, $CH_2{=}C$). Anal. Calcd for $C_{19}H_{33}OSBF_4{\cdot}1/4H_2O$: C, 56.71; H, 8.43. Found: C, 56.64; H, 8.39.

(2*R*)-2,3-Epoxy-3-methylbutanal 24 CrO_3 (14.4 g, 0.13 mol) was added to a solution of pyridine (17 mL, 0.22 mol) in CH_2Cl_2 (200 mL) at 0 °C and the mixture was stirred at rt for 30 min. After addition of dry celite (70 g), (2*S*)-2,3-epoxy-3-methylbutan-1-ol[12] (2.4 g, 14 mmol) was added. The mixture was stirred at rt for 20 min. After addition of a mixture of ether and pentane (1:1, 170 mL), $MgSO_4$ (40 g), and $NaHSO_4{\cdot}H_2O$ (40 g), the mixture was filtered through florisil. The filtrate was concentrated to about 20 mL. Distillation (rt/3 mmHg) gave 40% ether solution of **24** (2.5 g, 42%). NMR δ: 1.38, 1.42 (each 3H, s, CH_3), 3.10 (1H, d, J=6 Hz, CHCHO), 9.30 (1H, d, J=6 Hz, CHCHO).

Generation of ylide from (+)-11 and coupling with 24 providing (+)-1 MeLi (0.86 M in ether, 0.80 mL, 0.69 mmol) was added to a solution of (+)-**11** (111 mg, 0.28 mmol) and HMPA (0.053 mL, 0.30 mmol) in DME (20 mL) at -70 °C, and the mixture was stirred at -70 °C for 1 h. To this solution, **24** (40% in ether, 0.3 g, 1.2 mmol) in DME (1 mL) was added at -70 °C, the whole was stirred at -70 °C for 50 min, at rt for 1 h, and cooled to -50 °C. After addition of pH 7 phosphate buffer, the mixture was extracted with CH_2Cl_2 (20 mL x 3), and the combined extracts were dried. Concentration and chromatography (AcOEt-hexane 1:3) gave **34** (20 mg, 35%) as a colorless oil and the mixture of **1**, **32**, and **33** (18 mg) as an oil. Separation of the mixture of **1**, **32**, and **33** by HPLC (Waters Radial Pak B, acetone-hexane 1:6) afforded (+)-**1** (2 mg, 3%) as colorless solid, (+)-**32** (1.5 mg, 1.5%) as a colorless oil, and (+)-**33** (5 mg, 8%) as a colorless oil. (+)-**1**: mp 100-101 °C (colorless needles from petroleum ether). $[\alpha]_D^{23}$ +45.5 °(c 1.23, $CHCl_3$). IR (nujol): 3360, 1635 cm^{-1}. NMR δ: 0.93 (3H, d, J=6 Hz, CH_3), 1.01, 1.32, 1.43 (each 3H, s, CH_3), 1.1-2.2 (10H, m), 2.31 (1H, dt, J=4, 13 Hz, $CH_2CHC{=}CH_2$), 2.51 (1H, d, J=8 Hz, $(CH_3)_2C(O)CH$), 2.90 (1H, dd, J=8, 4 Hz, $(CH_3)_2C(O)CHCH(O)CH$), 2.9-3.2 (1H, m), 3.47 (1H, dd, J=4, 0.8 Hz, $(CH_3)_2C(O)CHCH(O)CH$), 3.76 (1H, d, J=4 Hz, HOCH), 5.05, 5.16 (each 1H, t, J=1.4 Hz, $CH_2{=}C$). MS m/z: 318 (M^+). (+)-**32**: $[\alpha]_D^{23}$ +11 °(c 0.65, $CHCl_3$). IR (KBr): 3360 cm^{-1}. NMR δ: 0.93 (3H, d, J=8 Hz, CH_3), 1.01, 1.29, 1.39 (each 3H, s, CH_3), 1.1-2.4 (11H, m), 2.57 (1H, d, J=7 Hz, $(CH_3)_2C(O)CH$), 2.94 (1H, dd, J=7, 4 Hz, $(CH_3)_2C(O)CHCH(O)CH$), 2.9-3.3 (1H, m), 3.51 (1H, dd, J=4, 1 Hz, $(CH_3)_2C(O)CHCH(O)CH$), 3.77 (1H, d, J=4 Hz, HOCH), 5.05 and 5.14 (each 1H, dd, J=1, 3 Hz, $CH_2{=}C$). MS m/z: 318 (M^+). (+)-**33**: $[\alpha]_D^{23}$ +24.0 °(c 1.00, $CHCl_3$). IR (neat): 3440, 3100, 1640 cm^{-1}. NMR δ: 0.89 (3H, d, J=6 Hz, CH_3), 0.99,1.35, 1.40 (each 3H, s, CH_3), 1.1-2.2 (11H, m), 2.57 (1H, d, J=7 Hz, $(CH_3)_2C(O)CH$), 2.83 (1H, dd, J=7, 2 Hz, $(CH_3)_2C(O)CHCH(O)CH$), 2.8-3.1 (1H, m), 3.33 (1H, d, J=2 Hz, $(CH_3)_2C(O)CHCH(O)CH$), 3.75 (1H, d, J=4 Hz, HOCH), 4.97 and 5.20 (each 1H, s, $CH_2{=}C$). MS m/z: 318 (M^+). (+)-**34**: $[\alpha]_D^{24}$ +30.0 °(c 0.26, $CHCl_3$). IR (neat): 3440, 3080, 1635 cm^{-1}. NMR δ: 0.91 (3H, d, J=6 Hz, CH_3), 1.01 (3H, s, CH_3), 1.1-2.7 (21H, m), 2.8-3.2 (2H, m), 3.75 (1H, d, J=4 Hz, HOCH), 4.7-5.0 (2H, m). MS m/z: 308 (M^+).

References and Notes

1. Stereoselective Reactions. Part 26. For the part 25, see: Tanaka, M.; Tomioka, K.; Koga, K. preceding paper.

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20. The *trans*-isomer was produced as a single isomer (the relative configuration was not determined)
21. The 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. Infrared 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. $CDCl_3$ was used as a solvent. Chemical shifts are expressed in ppm relative to internal Me_4Si. Abbreviations are as follows: s, singlet; t, triplet; q, quartet; m, multiplet; br, broad. Mass spectra (MS) were taken with a JEOL JMS DX-300 MS spectrometer.

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