Tetrahedron Vol 45, No 13, pp 4113 to 4124, 1989
Printed in Great Britain

0040-4020/89 $3 00+.0

TOTAL SYNTHESIS OF RACEMIC SELINA-3,7(11)-DIENE, α-SELINENE, AND α-EUDESMOL

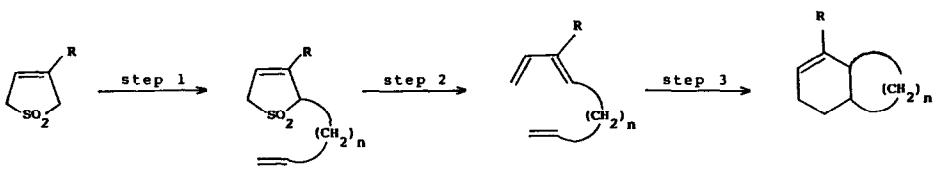
Ta-shue Chou*[a,b] , Shwu-Jiuan Lee[a] , and Nai-Kwang Yao[b]

a. Institute of Chemistry , Academia Sinica, Nankang, Taipei, Taiwan, Republic of China
b. Department of Chemistry, National Taiwan University, Taipei, Taiwan, Republic of China

(*Recewed in Japan* 23 *December* 1988)

Abstract: Three natural products of the eudesmane family, selina-3,7(11)-diene, α-selinene, and α-eudesmol, have been synthesized using a common strategy. The key steps involved in the strategy include the direct deprotonation/alkylation of isoprenyl sulfone and the intramolecular Diels-Alder reaction.

Recently, the study of using 3-sulfolenes as anionic and cationic butadienyl equivalents in organic synthesis has drawn increasing attention.[1] These reactions not only have been used to prepare a variety of substituted butadienes, but also have been utilized in the construction of hydronaphthalenes and hydroindanes via intramolecular Diels-Alder reactions[1c,d,h,p] (eq 1).

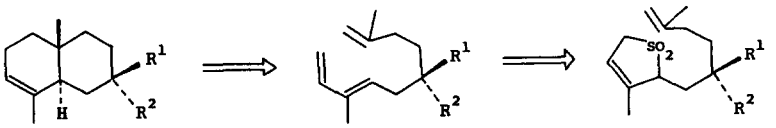


n= 3 or 4 (eq 1)

Owing to the high regioselectivity of the deprotonation/alkylation reaction giving 2-alkylated 3-sulfolenes (step 1 in eq 1), the stereospecificity of SO_2 extrusion giving E-dienes (step 2), and the stereoselectivity of the intramolecular Diels-Alder reaction giving trans-fused bicyclic systems, we expected that the reaction sequence shown in eq 1 should provide a very facile entry to the total synthesis of several sesquiterpenes of the eudesmane family.[2] Each of these natural products contains a trans-fused hydronaphthalene skeleton possessing an angular methyl group.

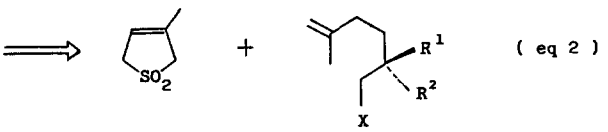
The target molecules chosen for this study are selina-3,7(11)-diene (1), α-selinene (2), and α-eudesmol (3).[3] Retrosynthetically (eq 2), the bicyclic skeleton of these compounds can be constructed via an intramolecular Diels-Alder reaction of the triene 4. The intramolecular Diels-Alder reaction of some similar systems has been shown to afford mainly trans-fused cycloadducts.[4] The precursor of triene 4, the properly substituted sulfolene 5, can be prepared by

the well-established deprotonation/alkylation sequence[1] from the commercially available isoprenyl sulfone 6 and an alkenyl halide 7.



1 R^1,R^2= isopropylidene
2 R^1= isopropenyl, R^2= H
3 R^1= 1-hydroxyisopropyl, R^2= H

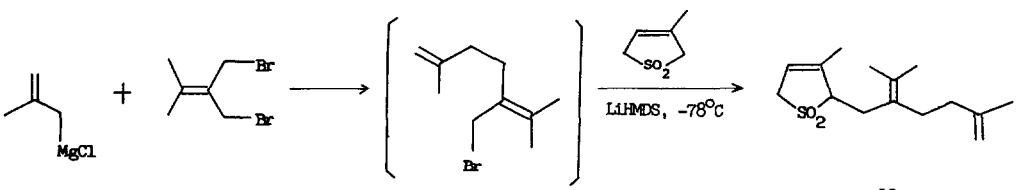
4 5



(eq 2)

6 7

Selina-3,7(11)-diene (1) appeared to us the simplest among the three[5] since the requisite alkenyl halide 10 for the deprotonation/alkylation step should be easily prepared by a cross-coupling of a methallyl carbanion and 2-isopropylidene-1,3-dibromopropane 9 (eq 3).[6]



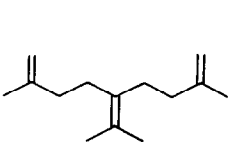
8 9 10 12

(eq 3)

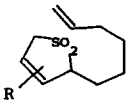
Thus, methallylmagnesium chloride 8, generated in THF at 5°C, reacted smoothly with 1 equiv of the dibromide 9 to give 10. By GC and ^{1}H NMR analysis, it was found that, in addition to 10, unreacted 9 and the doubly coupled product 11 were also present in the product mixture. Owing to the instability of the allylic bromide 10, attempted separation of it from other components resulted in serious decomposition and thus the characterization of 10 was extremely difficult. Fortunately, the crude product mixture from the cross coupling reaction could be used directly and it remained unchanged at -20°C for at least one week.

In the alkylation step, isoprenyl sulfone 6 and HMPA were mixed with the crude product containing 9, 10, and 11 followed by the addition of lithium hexamethyldisilazide at -78°C. In this way, the anion of isoprene sulfone 6 generated in situ could react instantaneously with the bromide 10 giving 12.

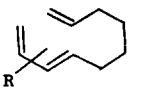
Separation of **11** from side products could be easily achieved by HPLC. The total yield up to this stage is 31% based on the amount of base used.



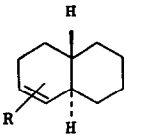
11



13

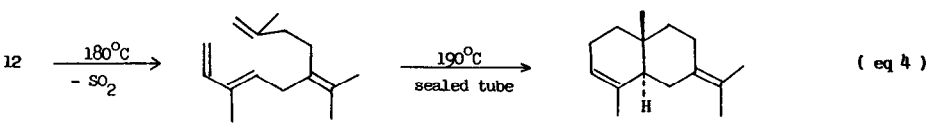


14



15

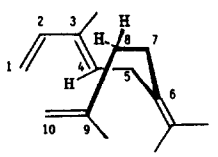
Since it has been established that the direct thermolysis of 2-(5-hexenyl)-3-sulfolene **13** at 580°C could yield the desired hydronaphthalene **15** without having to isolate the intermediate triene **14**,[1c,d] we treated compound **12** at first under high-temperature conditions (550-600°C) hoping to obtain **1** in a single step. Although **1** was produced in about 60% yield, it was accompanied with several unidentified side products which were difficult to separate. Stepwise thermolysis was then carried out where **12** was at first heated through a hot tube at 180°C giving the tetraene **16** (eq 4) in almost quantitative yield. Spectroscopic and chromatographic analysis revealed **16** as a single isomer and it was hence assigned to have an E-configuration between C3 and C4.[7] After a brief concentration under vacuum, **16** was immediately dissolved as a dilute solution of toluene and then heated in a sealed tube at 190°C for 110 hr. The intramolecular Diels-Alder reaction gave mainly one product which was identified to be selina-3,7(11)-diene (**1**) by IR, NMR, and MS comparison with literature.[2c,d] Thus, **1** was synthesized in only three steps.



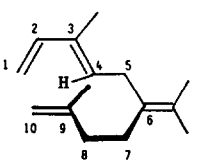
(eq 4)

16 1

The stereoselectivity of the intramolecular cycloaddition of **16** is remarkable. This is understandable by noting that, in the transition state **16A** leading to the cis-fused product, there is an unfavorable interaction between the methyl group on C3 and the substituent on C8, whereas the interaction is absent in the transition state **16B** leading to the trans-fused product.



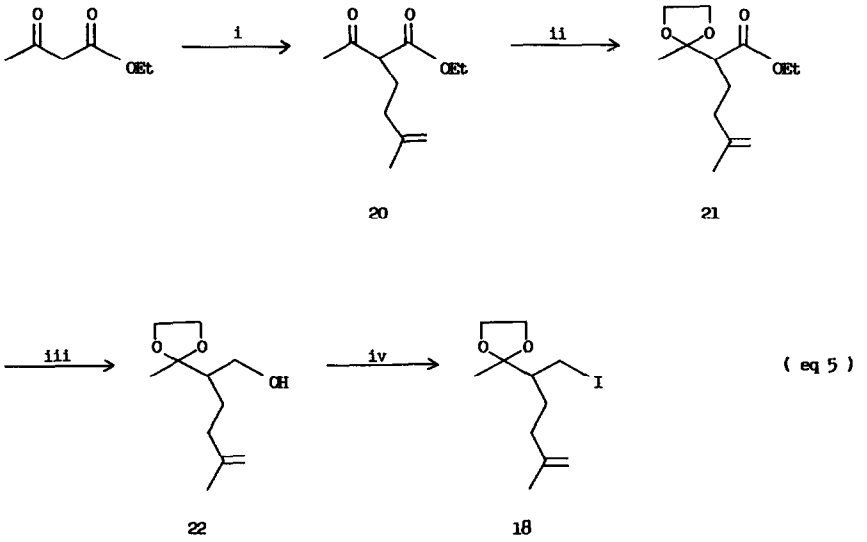
16 A



16 B

The other two sesquiterpenes **2** and **3** may be synthesized via a common intermediate **17**. Therefore, our next goal was to synthesize **17** by the strategy shown in eq 2. The requisite alkenyl halide for the ultimate preparation of **17** is **18** where the ketone must be protected so as to avoid possible side reactions

during the deprotonation/alkylation stage. Compound 17 could be easily prepared from the readily available iodide 19[3d] and ethyl acetoacetate by the classical reactions shown in eq 5.



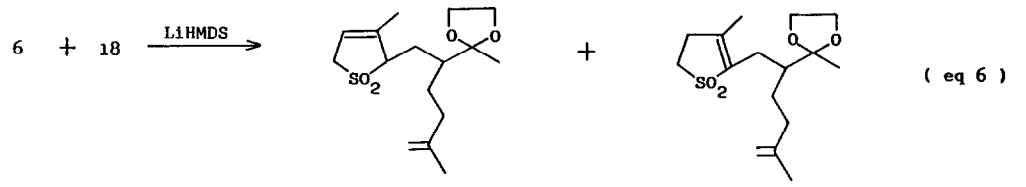
20 21 22 18 (eq 5)

Reagents: i, EtONa, 1-iodo-3-methyl-3-butene (19); ii, ethylene glycol, PPTS; iii, $LiAlH_4$; iv, PPh_3I_2.

Alkylation of the sodioacetoacetate with 19 smoothly produced 20. The protection of the ketone functionality to 21 was achieved with ethylene glycol using pyridinium p-toluenesulfonate (PPTS) in refluxing benzene.[8] Attempted ketalization reactions by using several other acid catalysts including TsOH, glutaric acid, stannic chloride, and pyridinium hydrochloride were not satisfactory probably owing to their high acidity which might cause side reactions at the C-C double bond site. Lithium aluminum hydride reduction of the ester functional group and subsequent treatment of the alcohol 22 with diiodotriphenylphosphorane[9] gave the desired alkyl iodide 18.

Deprotonation/alkylation reactions of 6 (2 equiv) with the iodide 18 (1 equiv) under standard condition,[1d] that is, with LiHMDS (1 equiv) at -78°C for 1-2 hr, gave the desired product 17 only in low yields (eq 6). A large quantity of its double bond isomer 23 (ca 40%) and some unreacted iodide 18 (ca 30%) in addition to the excess of isoprenyl sulfone 6 were present in the product mixture. Prolonged reaction (3 hr) increased the consumption of the iodide 18 (19% left unreacted), but the quantity of isomerized product 23 was also increased up to 60%. On the other hand, shortened reaction time (30 min) could minimize the isomerization, but the reaction proceeded only up to 20% leaving about 80% of the iodide 18 unreacted. Presumably, the alkylation reaction of the sulfolene anion of 6 with 18 is much slower than those for n-alkyl iodide so that the competition between alkylation of sulfolene anion and the double bond isomerization of the alkylated sulfolene 17 becomes a serious problem.[1b,g] Prolonged reaction would increase the extent of both reactions but gave no net

increase in the yield of **17**. Therefore, large excesses of sulfolene **6** and iodide **18** had to be used so as to enhance the rate of alkylation while leaving that of the isomerization reaction unaffected. The reaction of **6** (7.5 equiv) and iodide **18** (4 equiv) using LiHMDS (1 equiv) at -78°C for 2 hr appeared to be optimal. The desired product **17** was produced in 51% based on the consumed iodide **18**. The unreacted sulfolene **6** and iodide **18** could be recycled. Attempts for the isomerization of **23** back to **17** by deprotonation followed by kinetic protonation were unsuccessful.



(eq 6)

17 23

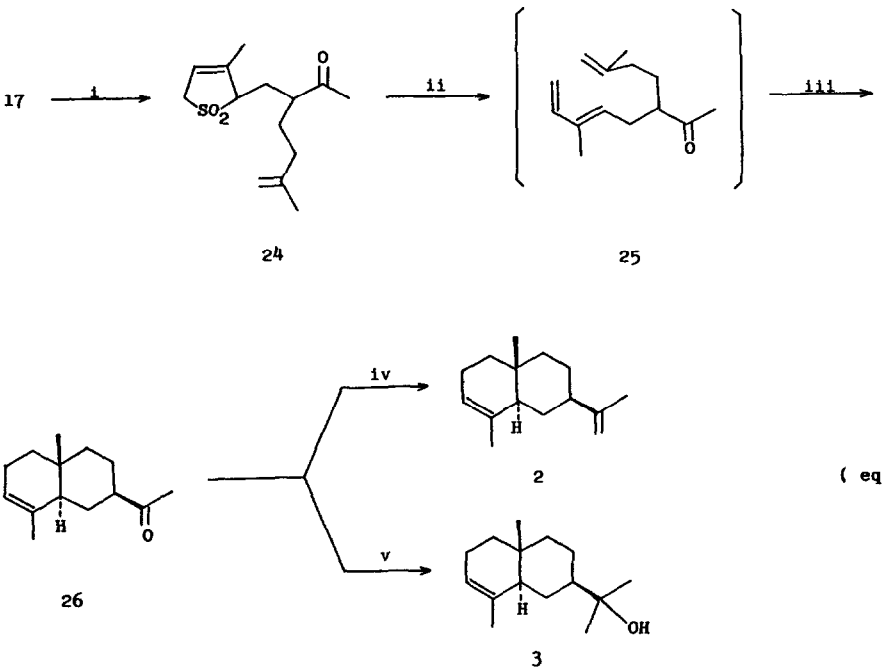
Compound **17** was found to exist as a mixture of two diastereomers which could be separated. However, since the subsequent thermal extrusion of SO_2 from **17** would eliminate the chiral center at the C2 of the sulfolene moiety, the stereochemistry of these two diastereomers was not determined. Either of the isolated diastereomers or a mixture of them could be used to give the same results.

Similar to the result of the high-temperature thermolysis of **12**, heating **17** at 580°C gave a complex mixture from which the separation of the components was extremely difficult. Heating **17** at 190°C in a sealed tube with or without the presence of pyridine[13] gave also a mixture of decomposed products. It was then expected that a deketalization reaction of **17** prior to thermolysis might probably work better. Deprotection of **17** could be achieved by stirring in acetone with a catalytic amount of TsOH to give **24** (eq 7) in almost quantitative yield. Compound **24** existed as a mixture of diastereomers of which the separation was unnecessary. A rapid pyrolysis of **24** at 350°C extruded SO_2 to give the corresponding trienone **25** presumably in the E-form. A solution of **25** in toluene was immediately thermolyzed at 170°C for 3 days in a sealed tube. The desired cycloadduct **26** was produced in 42% along with some other unidentified yet separable side products. Attempts to increase the yield of **26** by varying the reaction temperature or the concentration of **25** in thermolysis were unsuccessful. The relative stereochemistry of the three chiral centers of **26** was not determined at this stage. But they were believed to be those as shown in the structure drawn in eq 7 because of the successful transformation of it to the natural products **2** and **3**.

The remaining steps were easy to carry out. Treatment of **26** with methylene phosphorane gave α-selinene (**2**) and treatment of **26** with methyl Grignard gave α-eudesmol (**3**) in excellent yields. The structure of **2** was confirmed by comparison of the IR and NMR spectra with those in literature[2e] while that of **3** was confirmed by comparison of the IR and NMR spectral data with those in literature.[3a,b,e]

Although the intramolecular Diels-Alder reaction has been used extensively

in the total synthesis of natural products,[4] the requisite trienes for these reactions are in general prepared by multistep reactions and, sometimes, with difficulty. The strategy described in this paper for the synthesis of sesquiterpenes 1, 2, and 3 is highly convergent where the two parts of the triene precursors are put together by a simple carbanion alkylation process. For this reason, the target molecules are prepared very efficiently.



(eq 7)

Reagents: i, TsOH, $(CH_3)_2CO$; ii, 350°C; iii, toluene, sealed tube, 170°C; iv, Ph_3PCH_2; v, CH_3MgBr.

Experimental Section

General Method. NMR spectra were determined on a Brucker AW-80, or a Brucker MSL-200 spectrometer as solution in $CDCl_3$ unless otherwise noted. IR spectra were determined on a Perkin-Elmer 882 IR spectrophotometer. Mass spectra were recorded on a Hewlett-Packard 5995B GC/MS spectrometer. High resolution mass spectra were recorded on a Jeol JMS-D300 GC/MS spectrometer. Elemental analyses were performed at the microanalysis laboratory of National Taiwan University using a Perkin-Elmer 240C analyzer. All reactions were performed under an atmosphere of dry nitrogen. All anhydrous solvents were freshly distilled before use.

2-(2-Isopropylidene-5-methyl-5-hexenyl)-3-methyl-3-sulfolene (12). To a solution of 2-isopropylidene-1,3-dibromopropane (9) (1.14 g, 4.7 mmol) in ether (22 mL) at -10°C was added methallylmagnesium chloride (6.4 mL, 0.8 M, prepared

from magnesium power and methallyl chloride at 5°C) dropwise during a period of 1 hr. After the addition was complete, cuprous iodide (89.5 mg, 0.47 mmol) was added to the reaction mixture. The resulting mixture was stirred at 0°C for 15 hr, whereupon saturated ammonium chloride was added and then extracted with ether (25 mL x 3). The combined organic layers were washed with saturated brine and dried ($MgSO_4$). The solvent was removed under reduced pressure and the crude oily mixture containing 9, 10, and 11 was obtained (908 mg).

To a mixture of 3-methyl-3-sulfolene (6) (198 mg, 1.5 mmol), the crude mixture prepared as described above, and hexamethylphosphoramide (HMPA, 538 mg, 3 mmol) in THF (10 mL) at -78°C was added LiHMDS [0.75 mmol, prepared from hexamethyldisilazane (1.2 mmol) and n-butyllithium (0.75 mmol) at 0°C] dropwise during a period of 20 min. The resulting mixture was stirred at -78°C for 1 hr, whereupon n-hexane/EtOAc (1:1, 10 mL) was added. The precipitate was filtered off and the excess of solvent was evaporated under reduced pressure. The crude product was eluted through a silica gel column (n-hexane/EtOAc 2:1) to remove HMPA. The crude product was purified by HPLC (LiChrosorb column, n-hexane/EtOAc 2:1) to give 12 (62.3 mg, 31% yield based on LiHMDS used). Compound 12 : colorless oil; IR (neat) 3074, 2920, 1648, 1444, 1308, 1245, 1204, 1150, 1112, 885 cm^{-1}; ^1H NMR (200 MHz) δ 1.63 (s, 6 H), 1.69 (s, 3 H), 1.76 (s, 3 H), 1.93-2.20 (m, 4 H), 2.39 (dd, 1 H, J = 14, 9 Hz), 2.64 (dd, 1 H, J = 14, 6 Hz), 3.50 (dd, 1 H, J = 9, 6 Hz), 3.62 (br s, 2 H), 4.64 (br s, 2 H), 5.61 (s, 1 H); MS m/z 268 (M^+), 225, 203, 148, 147, 133 (100%), 119, 107, 105, 93, 91, 55, 41. Anal. Calcd for $C_{15}H_{24}O_2S$: C, 67.12; H, 9.01. Found: C, 66.86; H, 9.30.

3,9-Dimethyl-6-isopropylidene-1,3,9-decatriene (16). A solution of 12 (34 mg, 0.127 mmol) in completely degassed n-hexane (18 mL) was passed dropwise through a hot tube at 180°C under nitrogen (contact time 35 sec) for 50 min. The condensate was collected and the solvent was removed under reduced pressure giving the essentially pure tetraene 16 in almost quantitative yield. Analytical sample was obtained by purification with HPLC (LiChrosorb column). Compound 16 : colorless oil; IR (neat) : 3075, 2964, 1648, 1607, 1445, 1261, 1096, 1024, 887, 801 cm^{-1}; ^1H NMR (200 MHz) δ 1.57 (s, 6 H), 1.66 (s, 3 H), 1.72 (s, 3 H), 1.89-2.08 (m, 4 H), 2.81 (d, 2 H, J = 7 Hz), 4.61 (br s, 2 H), 4.85 (d, 1 H, J = 11 Hz), 5.01 (d, 1 H, J = 17 Hz), 5.33 (t, 1 H, J = 7 Hz), 6.30 (dd, 1 H, J = 11, 17 Hz); ^{13}C NMR (50.33 MHz) δ 11.65, 20.15, 20.30, 22.38, 31.26, 31.39, 36.55, 109.44, 110.29, 125.66, 130.55, 131.83, 133.52, 141.50, 146,21; MS m/z 204 (M^+), 148, 147, 133, 121, 119, 107, 105, 93, 91, 84, 81, 77, 69, 55, 53, 43, 41 (100%).

Selina-3,7(11)-diene (1). A solution of 16 (16 mg, 0.078 mmol) in completely degassed toluene (2.2 mL) was heated to 190°C in a sealed tube for 110 hr. The solvent was removed under reduced pressure, and the crude product was purified by HPLC (LiChrosorb column, n-hexane) to give 1 in 75% yield and 16 in 20%. Compound 1 : colorless oil; IR (neat) 2963, 2912, 2850, 1649, 1452, 1374, 1260, 1220, 1171, 1088, 1017, 798 cm^{-1}; ^1H NMR (80 MHz, CCl_4) δ 0.83 (s, 3 H), 1.01-1.40 (m, 4 H), 1.64 (br s, 9 H), 1.80-2.80 (m, 7 H), 5.26 (br s, 1 H); ^{13}C NMR (50.33 MHz) δ 15.06, 19.97, 20.09, 20.97, 22.92, 25.19, 27.36, 32.22, 37.69, 40.63, 46.98, 121.11, 121.29, 131.43, 135.07; MS m/z 204 (M^+), 189, 161 (100%), 133, 122, 119, 107, 105, 93, 91, 79, 55, 41. The ^1H NMR,

IR and MS spectra were identical with literature spectra.[2d]

Ethyl-2-acetyl-5-methyl-5-hexenoate (20). To a solution of sodium (0.57 g, 24.79 mmol) in absolute ethanol (50 mL) were added ethyl acetoacetate (3.89 g, 29.88 mmol) and 1-iodo-3-methyl-3-butene (19)[3d] (5.37 g, 27.39 mmol) sequentially. The mixture was refluxed for 10 hr. The resulting mixture was washed with 1 N H_2SO_4 and then extracted with chloroform (30 mL x 3). The combined organic layers were dried ($MgSO_4$) and concentrated under reduced pressure. The crude product was eluted through a silica gel column (n-hexane/EtOAc 10:1) to give **20** (4.20 g, 76% yield). Compound **20** : colorless oil; IR (neat) : 2980, 2890, 1738, 1721, 1648, 892 cm^{-1}; ^1H NMR (200 MHz) δ 1.28 (t, 3 H, J = 6 Hz), 1.71 (s, 3 H), 1.98-2.10 (m, 4 H), 2.23 (s, 3 H), 3.43 (s, 1 H), 4.20 (q, 2 H, J = 6 Hz), 4.70 (s, 1 H), 4.74 (s, 1 H); MS m/z 198 (M^+), 130, 55, 43 (100%).

Ethyl 2-(3-methyl-3-butenyl)-3-(ethylenedioxy)butanoate (21). To a solution of **20** (800 mg, 4.03 mmol) in benzene (25 mL) was added ethylene glycol (2.23 g, 36 mmol) and PPTS (251 mg, 1 mmol). The mixture was refluxed for 50 hr under a Dean-Stark trap for continuous removal of water. The resulting mixture was washed with saturated sodium bicarbonate and saturated brine. The organic phase was dried ($MgSO_4$) and concentrated under reduced pressure. The crude product was eluted through a silica gel column (n-hexane/EtOAc 7:1) to give **21** (830 mg, 85% yield). Compound **21** : colorless oil; IR (neat) 2984, 2890, 1731, 1646, 1446, 1376, 1243, 884 cm^{-1}; ^1H NMR (200 MHz) δ 1.21 (t, 3 H, J = 7 Hz), 1.34 (s, 3 H), 1.64 (s, 3 H), 1.70-2.10 (m, 4 H), 2.53-2.69 (m, 1 H), 3.89 (s, 4 H), 4.11 (q, 2 H, J = 7 Hz), 4.62 (s, 1 H), 4.66 (s, 1 H); MS m/z 242 (M^+), 87 (100%), 43. Anal. Calcd for $C_{13}H_{22}O_4$: C, 64.44; H, 9.15. Found : C, 64.41; H, 9.10.

2-(Ethylenedioxy)-3-(hydroxymethyl)-6-methyl-6-heptene (22). To a suspension of lithium aluminum hydride (430 mg, 11.3 mmol) in THF (30 mL) at 0°C was added **21** (2.38 g, 9.51 mmol) in THF (10 mL) dropwise. The mixture was stirred for 2 hr and acetone was added to destroy the excess of $LiAlH_4$. The resulting mixture was poured into saturated brine and then extracted with ethyl acetate (40 mL x 3). The combined organic layers were dried ($MgSO_4$) and concentrated under reduced pressure. The crude product was eluted through a silica gel column (n-hexane/EtOAc 4:1) to give **22** (1.69 g, 89% yield). Compound **22** : colorless oil; IR (neat) 3510, 2889, 1654, 1445, 1150, 1043, 885 cm^{-1}; ^1H NMR (200 MHz) δ 1.30 (s, 3 H), 1.71 (s, 3 H), 1.75-1.80 (m, 3H), 2.06 (q, 2 H, J = 6 Hz), 3.13 (s, 1 H), 3.64 (d, 2 H, J = 6 Hz), 3.97 (s, 4 H), 4.70 (s, 2 H); MS m/z 200 (M^+), 87 (100%), 43. Calcd for $C_{11}H_{20}O_3$: 200.1412. Found : m/z 200.1395.

2-(Ethylenedioxy)-3-(iodomethyl)-6-methyl-6-heptene (18). To a solution of triphenylphosphine (1.52 g, 5.80 mmol) in THF (30 mL) at 0°C was added iodine (1.62 g, 6.38 mmol), whereupon the color of the reaction mixture was turned into yellow. To the resulting mixture were added **22** (0.97 g, 4.83 mmol) in THF and pyridine (2 mL) sequentially. The mixture was stirred for 2 hr, whereupon methanol was added to quench the reaction. The precipitate was filtered off and the solvent was concentrated under reduced pressure. The crude product was eluted through a silica gel column (n-hexane/EtOAc 6:1) to give **18** (1.49 g, 99% yield). Compound **18** : colorless oil; IR (neat) 2984, 2895, 1653, 1447, 1206, 1045, 889 cm^{-1}; ^1H NMR (200 MHz) δ 1.31 (s, 3 H), 1.5-1.7 (m, 2 H), 1.75 (s,

3 H), 2.0-2.3 (m, 3 H), 3.0-3.5 (m, 2 H), 3.94 (s, 4 H), 4.72 (s, 2 H); MS m/z 310(M^+), 183, 87 (100%), 43. Anal. Calcd for $C_{11}H_{19}IO_2$: C, 42.59; H, 6.17. Found : C,42.61; H, 6.17.

2-[2-(3-methyl-3-butenyl)-3-(ethylenedioxy)butyl]-3-methyl-3-sulfolene (17) and **2-[2-(3-methyl)-3-butenyl)-3-(ethylenedioxy)-butyl]-3-methyl-2-sulfolene (23).** To a mixture of 3-methyl-3-sulfolene (6) (1.98 g, 15 mmol), 18 (2.48 g, 8 mmol), and HMPA (1.79 g, 10 mmol) in THF (60 mL) at -78°C was added LiHMDS (2 mmol) dropwise during a period of 15 min. The resulting mixture was stirred at -78°C for 90 min, whereupon ethyl acetate was added. The precipitate was filtered off and the excess of solvent was concentrated under reduced pressure. The crude product was eluted through a silica gel column (n-hexane/EtOAc 2:1) to give 17 (323 mg, 51.43% yield, based on LiHMDS used) and 23 (105 mg, 16.67% yield) and recovered 6 and 18. There are two diastereomers of 17 which are epimeric at the C2 of the sulfolene moiety. These two isomers were separated by HPLC (LiChrosorb column, n-hexane/EtOAc 2:1) in 5:2 ratio (17a : 17b) but the relative stereochemistry was not determined. **Compound 17a** (the faster moving isomer on HPLC) : colorless oil; IR (neat, mixture of 17a, 17b) 2939, 1648, 1449, 1305, 1121, 1037, 884, 791 cm^{-1}; ^1H NMR (80 MHz) δ 1.23 (s, 3 H), 1.70 (s, 3 H), 1.83 (s, 3 H), 1.83-2.40 (m, 7 H), 3.45 (s, 2 H), 3.89 (s, 4 H), 4.05 (br s, 1 H), 4.64 (s, 2 H), 5.58 (br s, 1 H); MS m/z 314 (M^+), 250, 87 (100%), 43, 41. Anal. Calcd for $C_{16}H_{26}O_4S$: C, 61.12; H, 8.33. Found : C, 61.16; H, 8.78. **Compound 17b** (the slower moving isomer on HPLC) : colorless oil; ^1H NMR (80 MHz) δ 1.23 (s, 3 H), 1.71 (s, 3 H), 1.80-2.40 (m, 10 H), 3.52 (br s, 3 H), 3.89 (s, 4 H), 4.65 (s, 2 H), 5.56 (br s, 1 H); MS m/z 314 (M^+), 250, 87 (100%), 43. **Compound 23** : colorless oil; IR (neat) 2941, 2885, 1648, 1442, 1138, 884, 789 cm^{-1}; ^1H NMR (200 MHz) δ 1.30 (s, 3 H), 1.70 (s, 3 H), 1.92 (s, 3 H), 1.9-2.4 (m, 7 H), 2.70 (t, 2 H, J = 6 Hz), 3.23 (t, 2 H, J = 6 Hz), 3.94 (s, 4 H), 4.66 (s, 2 H); MS m/z 314 (M^+), 87 (100%), 43, 41. Anal. Calcd for $C_{16}H_{26}O_4S$: C, 61.12; H, 8.33. Found : C, 61.22; H, 8.74.

2-(2-Acetyl-5-methyl-5-hexenyl)-3-methyl-3-sulfolene (24). A mixture containing 17 (264 mg, 0.84 mmol) and anhydrous acetone (30 mL) along with a catalytic amount of p-toluenesulfonic acid (50 mg) was stirred at room temperature for 7 hr. The resulting mixture was washed with saturated sodium bicarbonate and then extracted with $CHCl_3$ (20 mL x 3). The combined organic layers were dried ($MgSO_4$) and concentrated under reduced pressure to give 24 in quantitative yield. The two diastereomers of 24 were separated by a silica gel column (n-hexane/EtOAc 3:1) in 5:2 ratio (24a : 24b) but the relative stereochemistry was not determined. **Compound 24a** (the faster moving isomer on silica gel column) : colorless oil; IR (neat) 2929, 1713, 1650, 1443, 1305, 1116, 892, 789 cm^{-1}; ^1H NMR (80 MHz, CCl_4) δ 1.72 (s, 3 H), 1.88 (s, 3 H), 2.19 (s, 3 H), 1.8-2.2 (m, 6 H), 2.8-3.4 (m, 2 H), 3.58 (s, 2 H), 4.71 (s, 2 H), 5.54 (s, 1 H); MS m/z 270 (M^+), 206, 71, 43 (100%), 41. Anal. Calcd for $C_{14}H_{22}O_3S$: C, 62.19; H, 8.20. Found : C, 62.26; H, 8.67. **Compound 24b** (the slower moving isomer on silica gel column) : colorless oil; ^1H NMR (200 MHz) δ 1.72 (s, 3 H), 1.82 (s, 3 H), 1.85-2.20 (m, 6 H), 2.23 (s, 3 H), 2.86-3.05 (m, 1 H), 3.66-3.80 (m, 3 H), 4.69 (s, 1 H), 4.75 (s, 1 H), 5.69 (s, 1 H).

***trans*-1-Methyl-4'-methyl-7-acetyl-3,4,4',5,6,7,8,8'-octa-hydronaphthalene (26).** A solution of 24 (227 mg, 0.84 mmol) in completely degassed benzene

(27 mL) was passed dropwise through a hot tube at 350°C under nitrogen during a period of 85 min (contact time 30 sec). The resulting mixture was washed with saturated sodium carbonate. The organic phase was dried and concentrated under reduced pressure to give the crude trienone 25. ^{1}H NMR (200 MHz) δ 1.69 (s, 3 H), 1.74 (s, 3 H), 2.14 (s, 3 H), 1.80-2.57 (m, 7 H), 4.66 (s, 1 H), 4.72 (s, 1 H), 4.96 (d, 1 H, J = 11 Hz), 5.10 (d, 1 H, J = 17 Hz), 5.83 (t, 1 H, J = 7 Hz), 6.34 (dd, 1 H, J = 11, 17 Hz). Compound 25 thus prepared was dissolved with a trace amount of methylene blue (20 mg) in completely degassed toluene (15 mL) and was heated to 170°C in a sealed tube for 68 hr. The solvent was removed under reduced pressure and the crude product was purified by silica gel chromatography (n-hexane/EtOAc 30:1) to give 26 (73 mg, 42% yield from 24). **Compound 26** : colorless oil; IR (neat) 2930, 1712 cm^{-1}; ^{1}H NMR (200 MHz) δ 0.81 (s, 3 H), 0.85-1.55 (m, 8 H), 1.61 (s, 3 H), 1.65-2.00 (m, 3 H), 2.07 (s, 3 H), 2.23 (m, 1 H), 5.19 (s, 1 H); ^{13}C NMR (50.33 MHz) δ 22.44, 22.83, 23.91, 25.77, 26.61, 27.83, 31.02, 31.33, 39.85, 46.58, 51.91, 119.58, 135.88, 211.99; MS m/z 206 (M$^+$), 107, 93, 91 (100%), 43, 41.

***α*-Selinene (2).** To a solution of methyl triphenylphosphonium bromide (950 mg, 2.66 mmol) in THF (30 mL) at 0°C were added n-butyllithium (1.22 M, 1 mL, 1.22 mmol) and 26 (53 mg, 0.26 mmol) sequentially. The resulting mixture was stirred for 1 hr, whereupon acetone was added. The solvent was evaportated under reduced pressure. The residue was eluted through a silica gel column to remove triphenylphosphine oxide. The crude product was purified by HPLC (Chromosorb column, n-hexane/EtOAc 19:1) to give *α*-selinene (44 mg, 84% yield). **Compound 2** : colorless oil; IR (neat) 2924, 2851, 1645, 1456, 1438, 1377, 886 cm^{-1}; ^{1}H NMR (200 MHz) δ 0.79 (s, 3 H), 1.60 (s, 3 H), 1.72 (s, 3 H), 0.80-1.60 (m, 8 H), 1.75-2.00 (m, 4 H), 4.69 (s, 2 H), 5.29 (s, 1 H); ^{13}C NMR (50.33 MHz) δ 15.53, 20.79, 21.06, 22.89, 26.74, 28.82, 32.21, 37.87, 40.16, 46.63, 46.72, 108.14, 120.81, 135.01, 150.84; MS m/z 204 (M$^+$), 189, 147, 133, 122, 107, 93, 91, 79, 55, 41 (100%). The IR and ^{1}H NMR spectra are identical with literature.[2e]

***α*-Eudesmol (3).** To a solution of 26 (66 mg, 0.32 mmol) in THF (20 mL) at room temperature was added methylmagnesium bromide (3.0 M, 1 mL, 3 mmol). The mixture was stirred for 1 hr, whereupon methanol was added. The resulting mixture was washed with dilute sulfuric acid and then extracted with dichloromethane (20 mL x 2). The combined organic layers were dried ($MgSO_4$) and concentrated under reduced pressure. The crude product was purified by HPLC (Chromosorb column) to give 3 (67 mg, 94% yield). **Compound 3** : colorless oil; IR (neat) 3393, 2935, 1453, 1376, 1143, 798 cm^{-1}; ^{1}H NMR (200 MHz) δ 0.77 (s, 3 H), 1.20 (s, 3 H), 1.21 (s, 3 H), 1.25-1.60 (m, 8 H), 1.62 (s, 3 H), 1.65-2.10 (m, 5 H), 5.32 (s, 1 H); ^{13}C NMR (50.33 MHz) δ 15.43, 21.05, 22.29, 22.84, 24.21, 26.66, 27.44, 32.06, 37.72, 40.04, 46.51, 49.85, 72.89, 120.85, 135.02; MS m/z 222 (M$^+$), 204, 149, 107, 93, 91, 59 (100%), 43, 41. The IR and ^{1}H NMR spectral data are identical with those in literature.[3a,b,e]

Acknowledgment. We thank the National Science Council of the Republic of China for financial support.

References

1. (a) Chou, T.S.; Tso, H.H.; Chang, L.J. *J. Chem. Soc., Chem. Commun.* 1984, 1323. (b) Chou, T.S.; Tso, H.H.; Chang, L.J. *J. Chem. Soc., Perkin Trans. 1* 1985, 515. (c) Chou, T.S.; Tso, H.H.; Chang, L.J. *J. Chem. Soc., Chem. Commun.* 1985, 236. (d) Tso, H.H.; Chang, L.J.; Lin, L.C.; Chou, T.S. *J. Chin. Chem. Soc.* 1985, *32*, 333. (e) Chou, T.S.; Chang, L.J.; Tso, H.H.; *J. Chem. Soc., Perkin Trans 1* 1986, 1039. (f) Chou, T.S.; Tso, H.H.; Lin, L.C. *J. Org. Chem.* 1986, *51*, 1000. (g) Chou, T.S.; You, M.L. *Bull. Inst. Chem, Acad. Sin.* 1986, *33*, 13. (h) Tso, H.H.; Liu, L.T.; Lin, L.C.; Chou, T.S. *J. Chin. Chem. Soc.* 1986, *33*, 323. (i) Tao, Y.T.; Liu, C.L.; Lee, S.J.; Chou, S.S.P. *J. Org. Chem.* 1986, *51*, 4718. (j) Chou, T.S.; Tso, H.H.; Tao, Y.T.; Lin, L.C. *J. Org. Chem.* 1987, *52*, 244. (k) Tso, H.H.; Chou, T.S.; Lee, W.C. *J. Chem. Soc., Chem. Commun.* 1987, 934. (l) Chou, S.S.P.; Liu, S.Y.; Tsai, C.Y.; Wang, A.J. *J. Org. Chem.* 1987, *52*, 4468. (m) Chou, T.S.; Lee, S.J.; Tso, H.H.; Yu, C.F. *J. Org. Chem.* 1987, *52*, 5082. (n) Chou, T.S.; Hung, S.C.; Tso, H.H. *J. Org. Chem.* 1987, *52*, 3394. (o) Lee, S.J.; Chou, T.S.; Peng, M.L.; Ho. W.H. *Bull. Inst. Chem., Acad. Sin.* 1988, *35*, 1. (p) Tao, Y.T.; Chen, M.L. *J. Org. Chem.* 1988, *53*, 69. (q) Chou, T.S.; Hung, S.C. *J. Org. Chem.* 1988, *53*, 3020. (r) Chou, T.S.; Lee, S.J.; Peng, M.L.; Sun. D.J.; Chou, S.S.P. *J. Org. Chem.* 1988, *53*, 3027. (s) Yamada, S.; Ohsawa, H.; Suzuki, T.; Takayama, H. *Chem. Lett.* 1983, 1003. (t) Takayama, H.; Suzuki, H.; Nomoto, T.; Yamada, S. *Heterocycl.* 1986, *24*, 303. (u) Yamada, S.; Ohsawa, H.; Suzuki, T.; Takayama, H. *J. Org. Chem.* 1986, *51*, 4934. (v) Nomoto, T.; Takayama, H. *Heterocycl.* 1985, *23*, 2913. (w) Yamada, S.; Suzuki, H.; Naito, H.; Nomoto, T.; Takayama, H. *J. Chem. Soc., Chem. Commun.* 1987, 332.
2. (a) Heathcock, C.H. in " The Total Synthesis of Natural Products " vol 2, Chap 2., ApSimon, J., Ed.; Wiley & Sons : New York, 1973. (b) Heathcock, C.H.; Graham, S.L.; Pirrung, M.C.; Plavac, F.; White, C.T. " The Total Synthesis of Natural Products ", vol 5, ApSimon, J., Ed.; Wiley & Sons : New York, 1983. (c) Buttery, R.G.; Lundin, R.E.; Ling, L. *Chem. Ind. (London).* 1966, 1225. (d) Hartley, R.D.; Fawcett, C.H. *Phytochem.* 1969, *8*, 637. (e) Mauer, B.; Grieder, A. *Helv. Chim. Acta* 1977, *60*, 2177.
3. For successful examples of the partial and total synthesis of 1, 2, and 3, see (a) Humber, D.C.; Pinder, A.R. *Tetrahedron Lett.* 1966, 4985. (b) Humber, D.C.; Pinder, A.R.; Williams, R.A. *J. Org. Chem.* 1967, *32*, 2335. (c) Wilson, S.R.; Mao, D.T. *J. Am. Chem. Soc.* 1978, *100*, 6289. (d) Taber, D.F.; Saleh, S.A. *Tetrahedron Lett.* 1982, *23*, 2361. (e) Kutney, J.P.; Singh, A.K. *Can. J. Chem.* 1984, *62*, 1407. (f) Caine, D.; Stanhope, B. *Tetrahedron*, 1987, *43*, 5545. (g) Caine, D.; Stanhope, B.; Fiddler, S. *J. Org. Chem.* 1988, *53*, 4124.
4. For reviews in intramolecular Diels-Alder reactions, see (a) Oppolzer, W. *Angew. Chem. Int. Ed. Engl.* 1977, *16*, 10. (b) Brieger, G.; Bennett, J.N. *Chem. Rev.* 1980, *80*, 63. (c) Ciganek, E. *Organic Reactions* 1984, *32*, 1. (d) Fallis, A.G. *Can. J. Chem.* 1984, *62*, 183. (e) Taber, D.F. "Intramolecular Diels-Alder and Alder Ene Reactions", Springer-Verlag: New York, 1984. (f) Paquette, L.A. in "Asymmetric Synthesis", vol 3, Part B, Chap 7. Morrison, J.E. Ed.; Academic Press: New York, 1984.

5. The preliminary result of a facile synthesis of selina-3,7(11)-diene by this strategy has been published as a communication : Lee, S.J.; Chou, T.S. *J. Chem. Soc., Chem. Commun.* 1988, 1189.
6. Marshall, J.A.; Faubl, H.; Warne, T.M. *J. Chem. Soc., Chem. Commun.* 1967, 753.
7. (a) Mock, W.L. *J. Am. Chem. Soc.* 1975, *97*, 3666. (b) Kellogg, R.M.; Prins, W.L. *J. Org. Chem.* 1974, *39*, 2366. (c) McGregor, S.D.; Lemal, D.M. *J. Am. Chem. Soc.* 1966, *88*, 2858. (d) Cava, M.P.; Deana, A.A. *J. Am. Chem. Soc.* 1959, *81*, 4266.
8. (a) Miyashita, M.; Yoshikoshi, A.; Grieco, P.A. *J. Org. Chem.* 1977, *42*, 3772. (b) Sterzycki, R. *Synthesis* 1979, 724.
9. Schaefer, J.P.; Weinberg, D.S. *J. Org. Chem.* 1965, *30*, 2635.