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A NEW ROUTE FOR THE CONVERSION OF CARVONE INTO EUDESMANE SESQUITERPENES[1]

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Abstract. The β-hydroxy-α-phenylsulfenyl ketone **2**, derived from S-(+)-carvone, was treated with 2 equivalents of the Wittig-Horner phosphine oxide derivative **6** followed by excess methyl iodide to give a *ca.* 2 : 3 mixture of the E and Z α-phenylsulfenyl ketones **3a** and **3b**. The mixture of sulfides was oxidized to the corresponding sulfoxides **3c,d** with *m*-chloroperbenzoic acid. When this mixture refluxed in benzene, elimination of phenylsulfinic acid occurred and the intermediate E diene derivative **4a** underwent an intramolecular Diels-Alder reaction to give the *trans*-octalone **5a**, the *cis*-octalone **5c**, and another product believed to be the *trans*-octalone **5b** in a 60 : 28 : 12 ratio. The Z diene derivative **4b** was recovered under these reaction conditions. Wolff-Kishner reduction of the octalone mixture gave (-)-α-selinene (10) as the major product along with the *cis*-octalin **11** and other unidentified minor products. When the Z diene derivative **4b** was heated in toluene at 150°C for 48 h, a mixture of octalones having the same composition as that produced above was obtained. Likewise, when the 2 : 3 mixture of sulfoxides **3c** and **3d** was heated in toluene at 150°C, the same mixture of octalones was produced. Apparently, at the higher temperature, the Z diene derivative **4b** isomerized to the E isomer **4a** which ultimately underwent the intramolecular Diels-Alder reaction.

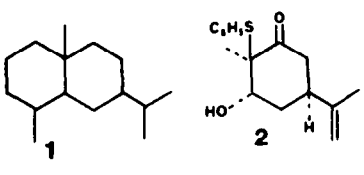
INTRODUCTION

Carvone and its derivatives have been widely used as the starting materials for enantiospecific syntheses of a variety of natural products including eudesmane sesquiterpenes.[2] Although the intermolecular Diels-Alder reaction of carvone and butadiene has been shown to provide octalone derivatives capable of conversion into eudesmane sesquiterpenes,[3] most of the reported conversions of carvone derivatives into these decalin ring systems have involved Robinson annelation sequences.[2] For example, we have reported an efficient synthesis of (+)-α-cyperone by a route involving stereoselective annelation of (-)-2-carone, which is readily made from (-)-carvone.[2c]

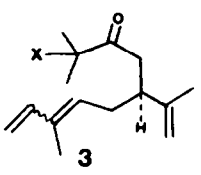
Recently, a new method for construction of decalin derivatives, including those having the eudesmane substitution pattern (cf. **1**), involving intramolecular Diels-Alder reactions of appropriate trienes or trienones has been developed by Taber and Saleh,[4] Wilson and Mao,[5] and others.[6] For example, Taber and Saleh have used the intramolecular Diels-Alder reaction of an acyclic triene containing a hydroxyisopropyl group at C-6 (numbering begins from the diene end of the chain) for the stereoselective synthesis of racemic α-eudesmol.[4] The bulky substituent on the triene caused substantial 1,3 and 1,4-chiral induction to produce the naturally occurring *trans* decalin ring system with the three-carbon substituent equatorial.

As has been pointed out by Taber and Saleh,[4] the use of enantiomerically pure acyclic precursors in intramolecular Diels-Alder reactions would allow the synthesis of optically active eudesmane sesquiterpenes. We wish to report a route for the synthesis of such compounds that begins with the β-hydroxy-α-phenylsulfenyl ketone **2**,[7] derived from S-(+)-carvone. In this approach, an E/Z mixture of acyclic α-phenylsulfenyl ketones

3a,b containing appropriately substituted conjugated diene moieties was generated from **2** by a tandem retroaldol-olefination-methylation sequence. Appropriate manipulations of the acyclic system yielded a mixture of unsaturated acyclic ketones (**4**) that underwent Diels-Alder cyclization to the target octalones **5**.

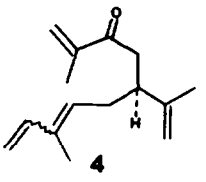


1 **2**



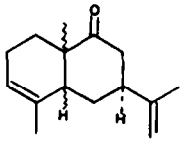
3

a. X = SC_6H_5; E conj. diene
b. X = SC_6H_5; Z conj. diene
c. X = SOC_6H_5; E conj. diene
d. X = SOC_6H_5; Z conj. diene



4

a. E conj. diene
b. Z conj. diene



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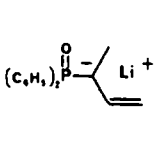
RESULTS AND DISCUSSION

Conjugated dienes with an E configuration are known to undergo intramolecular Diels-Alder reactions more smoothly than the corresponding Z isomers.[4c,6] Consequently, stereoselective conversion of β-ketol **2** into the E diene derivative **3a** was desirable. Yamamoto and coworkers[8] have shown that the Wittig-Horner reagent **6** reacts with simple aldehydes in tetrahydrofuran(THF)-hexamethylphosphoramide(HMPA) at low temperatures to give mixtures of 3-methyl conjugated dienes containing greater than 90% of the E isomer. Therefore, β-ketol **2** was treated with 2 equivalents of **6** in THF-HMPA at -78°C and the mixture was allowed to warm to 25°C over 0.5 h, cooled to 0°C and treated with 4.0 equivalents of methyl iodide. Upon workup, a mixture of isomers **3a,b** was isolated in 60% yield. Presumably, reagent **6** acts as a base to deprotonate the hydroxyl group and promote retroaldol cleavage of **2** to the aldehydo enolate **7a** that undergoes olefination at the aldehyde moiety with a second equivalent of **6** and methylation at the enolate moiety with methyl iodide.[7b] The C-2 proton of the vinyl group of the Z isomer in compounds such as **3** appears at lower field (*ca.* 6.6 δ) than the corresponding E isomer (*ca.* 6.4 δ).[8,9] Integration of the NMR spectrum of the E/Z mixture revealed that the E isomer **3a** and the Z isomer **3b** were present in a 1 : 9 ratio. Therefore, the reaction was stereoselective but in the undesired direction. By mixing 3-ketol **2** with reagent **6** at 0°C rather than -78°C and then conducting the methylation step as described above, the **3a** : **3b** ratio was increased to *ca.* 2 : 3, but other changes in the reaction conditions did not lead to improved stereoselectivity in favor of isomer **3a**.



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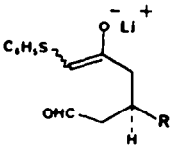
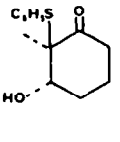


7

a. R = isopropenyl
b. R = H



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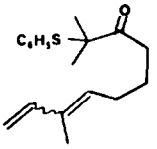

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a. E diene derivative
b. Z diene derivative

In order to gain a better understanding of the factors influencing the stereochemistry of the olefination step in the above reaction sequence, the β-ketol **8**, which contains no C-6 substituent, was prepared and reacted with reagent **6**. Under the low temperature conditions that yielded a 1 : 9 E/Z mixture from **2**, β-ketol **8** yielded a mixture of the E diene derivative **9a** and the Z diene derivative **9b** in a *ca.* 3 : 1 ratio. Thus, although the reaction of β-ketol **8** with reagent **6** was somewhat less stereoselective than that of simple aldehydes such as hexanal,[8] the E isomer was indeed favored in this case.

If one considers the intermediate aldehydo enolates **7** involved in these reactions, it appears that in going from the unsubstituted species **7b** to the 6-isopropenyl species **7a** the substituent has a profound effect on the stereoselectivity of the reaction. Yamamoto and coworkers[8] have suggested that E conjugated dienes arise from reactions of reagent **6** with simple aldehydes *via* thermodynamic control. However, examination of models does not provide an obvious reason why the C-6 isopropenyl group should cause the rates of formation or decomposition of the *erythro* adducts derived from reagent **6** and aldehydo enolate **7a** that lead to the Z diene **3b** to be so much faster than the corresponding reactions involving the *threo* adducts that lead to the E diene **3a**. An investigation of the reaction of **6** with simple aldehydes bearing β substituents that hopefully will shed light on this point is in progress.

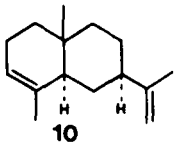
Treatment of the 2 : 3 mixture of **3a** and **3b** with *m*-chloroperbenzoic acid (MCPBA) in methylene chloride at -5°C for 15 min gave a crude mixture of the corresponding sulfoxides **3c** and **3d**. This mixture was heated in benzene at reflux for one hour to give a mixture of products that was separated into a mixture of octalones **5** (29% yield) and the uncyclized Z diene derivative **4b** (43% yield) by column chromatography on silica gel. Apparently, heating of the sulfoxide mixture caused elimination of phenylsulfinic acid[10] to give a mixture of the E and Z trienone derivatives **4a** and **4b** and the former isomer underwent an intramolecular Diels-Alder reaction under these conditions. Analysis of the mixture of octalones by gas chromatography using a crosslinked dimethyl silicone capillary column showed that three components that made up 60%, 28%, and 12% of the mixture were present. The major component was separated from the mixture of the two minor components by preparative gas chromatography using a 20% Silicone SE-30 on Chromosorb W column. Its infrared (IR) spectrum showed a strong absorption at 1720 cm^{-1} for a saturated carbonyl group in a six-membered ring and other absorptions expected for a trisubstituted double bond and a terminal disubstituted double bond. Its ^1H NMR spectrum showed a singlet at 1.08 δ for the angular methyl group, two broad singlets at 1.69 δ and 1.78 δ for the two vinyl methyl groups, a broad singlet at 4.79 δ for the terminal methylene group and a broad singlet at 5.38 δ for the vinyl hydrogen on the trisubstituted double bond. The IR and ^1H NMR spectra of the two-component mixture showed the expected absorptions for an isomeric mixture of octalones.

Previous investigations by Taber and coworkers[4] on intramolecular Diels-Alder reactions of related systems suggested that the major octalone formed from the E diene system **4a** should be the *trans*-octalone **5a**, while the middle component, i.e., the major component in the inseparable two-component mixture, should have the *cis*-octalone structure **5c**. Conclusive evidence for the structure of **5a** and additional support for the structure of **5c** was obtained as described below. The minor product which made up less than 12% of the octalone mixture could have structures **5b** or **5d**, but a firm assignment could not be made in this case.

The three-component mixture of octalones produced in the Diels-Alder reaction was subjected to Wolff-Kishner reduction using the conditions described by Nagata and Itazaki[11] for sterically hindered cyclic ketones. This gave a mixture of octalins (72% yield) that according to gas chromatographic analysis contained two major components that made up 45% and 35% of the reaction mixture, respectively, and at least four minor components, none of which amounted to as much as 10% of the total mixture.

The two major components were collected by preparative gas chromatography using a 20% Silicone SE-30 column. The component that was present in excess showed an optical rotation of $[\alpha]_D^{25} = -14.0^o$ ($CHCl_3$, 0.5%) which corresponded closely to the value of $[\alpha]_D^{25} = -14.5^o$ ($CHCl_3$, 1.0%) reported for (-)-α-selinene (**10**).[12] It also showed identical IR and ^1H NMR spectra to those reported for the sesquiterpene **10**.[12] Clearly, (-)-α-selinene was produced from Wolff-Kishner reduction of octalone **5a**. Thus, the exocyclic transition state A was the most favorable one for the intramolecular Diels-Alder cyclization of unsaturated ketone **4a** under thermal conditions.[4]

The second octalin isolated from the Wolff-Kishner reduction showed IR absorptions at 3080, 1665, 890, and 810 cm^{-1} for the terminal disubstituted and trisubstituted double bonds and its ^1H NMR spectrum showed a three-proton singlet at 0.87 δ for the angular methyl group, three-proton singlets at 1.66 δ and 1.72 δ for the two vinyl methyl groups, a broad singlet at 4.67 δ for the terminal methylene group, and a broad singlet at 5.24 δ for the vinyl hydrogen on the trisubstituted double bond. The assignment of the *cis* ring fusion to this compound was supported by the findings that (1) the peak width at half-height ($W_{h/2}$) for the angular methyl group was 0.66 Hz in the ^1H NMR spectrum and (2) the ^{13}C NMR absorption for the angular methyl group was at 27.0 δ. In (-)-α-selinene where there is a *trans* ring fusion the $W_{h/2}$ was 1.06 Hz for the angular methyl group in the ^1H NMR spectrum and this group absorbed at 15.6 δ in the ^{13}C NMR spectrum. In general, angular methyl ^1H NMR absorptions of *cis* decalins are narrower than the corresponding (absorptions for) *trans* isomers because the *cis* isomers have fewer possibilities for long-range coupling between the protons of the angular methyl group and protons on the ring carbons that can attain a W arrangement with them.[13] The lower field location of the angular methyl group absorptions in the ^{13}C NMR spectrum of *cis* as compared with *trans*-fused systems is attributable to the presence of fewer γ interactions with the ring carbon atoms that contribute to the shielding of the angular carbon atoms.[14]



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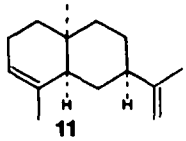

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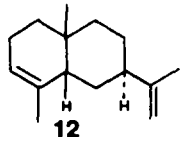
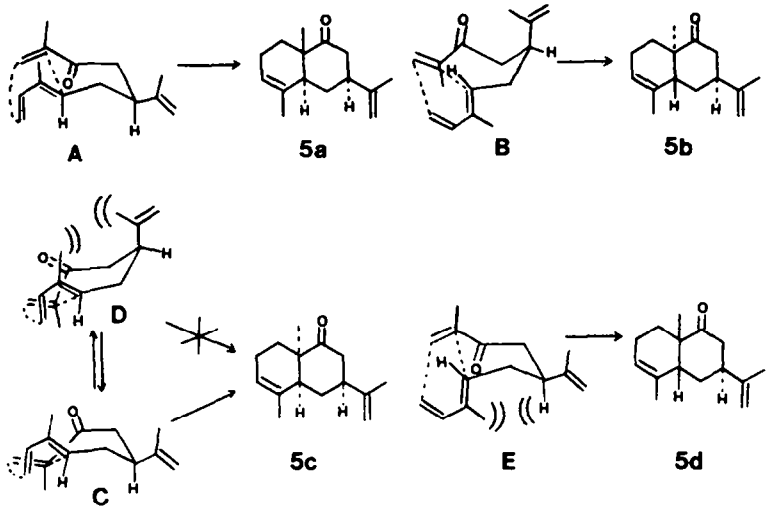


12

Possible structures for the *cis*-fused octalin isomer of (-)-α-selinene are **11** with a *trans* arrangement between the angular methyl group and the isopropenyl group and **12** in which these groups are *cis*. Since this hydrocarbon was derived from Wolff-Kishner reduction of the corresponding octalone **5c**, the major *cis*-fused product from the intramolecular Diels-Alder reaction, structure **11** should be the correct one. The preference for the formation of *cis*-octalone **5c**, which would yield compound **11**, over the *cis*-octalone **5d** in the intramolecular Diels-Alder reaction is based upon the fact that the chair-like *endo* transition state E has a severe interaction between the methyl group at C-3 and the hydrogen atom at C-6, which is not present in the boat-like

endo transition state C.[4] The chair-like *endo* transition state D could also lead to octalone **5c**, but it would be expected to be of very high energy because of the very severe steric interaction between the C-3 methyl group and the C-6 isopropenyl group.

Because neither the minor octalone from the intramolecular Diels-Alder reaction nor the minor octalin from the Wolff-Kishner reduction could be obtained pure, no definitive evidence for these structures was obtained. However, we suspect that the destablizing interaction between the C-3 methyl and the C-6 hydrogen which exists in the *endo* transition state E is severe enough to cause *exo* transition state B in which the isopropenyl group has an axial orientation with respect to the developing chair to be more stable. Therefore, the minor intramolecular Diels-Alder component probably has the *trans* structure **5b**.



Having established the course of the intramolecular Diels-Alder reaction of the E diene derivative **4a**, the behavior of the Z isomer **4b** was investigated. Surprisingly, when a solution of **4b** in toluene containing a trace of hydroquinone was heated in a sealed tube for 48 h at 150°C, a mixture of three octalones having an essentially identical composition to that produced from the E derivative **4a** was obtained. Transition states involving conversion of Z diene derivatives such as **4b** with four carbon atoms connecting the reacting centers into *trans*-fused octalones are highly strained and are unlikely to be involved.[6] Therefore, we feel that the most likely explanation for the above result is that the Z diene derivative **4b** underwent isomerization to the E isomer **4a** prior to cyclization.

Isomerization of Z dienes by thermally allowed 1,5-sigmatropic hydrogen migrations are known to be involved in certain intramolecular Diels-Alder reactions.[15] Conversions of less stable Z dienes into more stable E isomers by 1,5-sigmatropic hydrogen migrations followed by reversal of the process to move the double bonds back to their original positions are possible for many dienes.[15c] However, in the case of **4b** such rearrangements do not allow a change of configuration of the diene. Therefore, it seems likely that this Z to E conversion proceeds by another mechanism. Addition of a proton or a hydrogen atom to C-1 of **4b** would yield an allylic carbocation or allylic radical that could undergo rotation about the 3,4-bond and then lose a proton or hydrogen atom to give the isomer **4a**. The source of the proton or hydrogen atom donor could be hydroquinone or perhaps a trace of phenylsulfinic acid remaining after the thermolysis of the sulfoxide mixture.

It was also observed that when the 2 : 3 mixture of sulfoxides **3c** and **3d** was heated directly in toluene for 45 h at 150°C, the same mixture of octalones **5a** and **5c** plus the minor isomer was produced in 58% yield. Thus, the unexpectedly facile isomerization of **4b** to **4a** during heating allowed for the *trans*-octalone **5a** having the natural configuration of the eudesmane sesquiterpenes to be produced fairly efficiently in three steps, that is, (1) the retroaldol-olefination-methylation sequence, (2) oxidation of the acyclic sulfides to the corresponding sulfoxides, and (3) heating to effect elimination of the phenylsulfinic acid, isomerization of the Z diene, and the intramolecular Diels-Alder reaction.

EXPERIMENTAL

All reactions were carried out under a nitrogen atmosphere unless otherwise stated. Solvents and reagents were purified and dried by standard techniques. IR spectra were recorded on a Perkin-Elmer 283B spectrophotometer. ^{1}H NMR spectra were measured in $CDCl_3$ solutions at either 90 MHz on a Bruker WH-90 or at 200 MHz on a Nicolet 293A spectrometer. Chemical shifts are reported in δ units relative to internal Me_4Si. Mass spectra were measured at 70 eV on a Hewlett Packard Model 5985 spectrometer. Optical rotations were measured on a Perkin-Elmer 241 polarimeter in $CHCl_3$.

Flash column chromatography was carried out with E. Merck 60 silica gel (230-400 mesh). GLC analyses were recorded on a Hewlett-Packard 5790A spectrometer using a 12.5 m X 0.2 mm capillary column containing cross-linked dimethylsilicone. Gas chromatographic purification was carried out on a Varian Aerograph 90-P using a 10 ' X 0.25" stainless steel column containing 20% Silicone SE-30 on 80/100 mesh Chromosorb W. Elemental analyses were performed by Atlantic Microlab, Inc., Atlanta, GA. The high resolution mass spectrum was performed on a VG-ZAB-E ULTRA high resolution mass spectrometer by the Research Center for Biotechnology, Georgia Institute of Technology, Atlanta, GA.

1-Methyl-allyldiphenylphosphine oxide (6). A solution of 50.0 g (0.226 mol) of chlorodiphenylphosphine in 113.0 ml of ether was added slowly with stirring to a solution of 16.3 g (0.226 mol) of crotyl alcohol in 41.0 ml pyridine and 225 ml ether at 0°C. Stirring was continued for 3.0 h at 0°C and the mixture was filtered and the solvent removed from the filtrate under reduced pressure. The residue was then heated at 130°C for 2.0 h and upon cooling to room temperature crystallization occurred to give 42.4 g (73% yield) of 1-methylallydiphenylphosphine oxide (**6**), m.p. 85-88°C (lit.[16] 90-91°C). The IR and ^{1}H NMR spectra of the product were identical to those previously reported.[16]

Preparation of mixtures of E and Z Dienones 3a and 3b. To a solution of 23.96 g (0.0936 mol) of 1-methyl-allyldiphenylphosphine oxide (**6**) in 400 ml of anhydrous THF at -78°C was added 40.7 ml of a 2.3 M solution of *n*-butyllithium in hexanes. The mixture was stirred for 20 min at -78°C and allowed to warm to 0°C and treated with 67.1 g (0.374 mol) of dry HMPA. The mixture was stirred for 10 min and 10.76 g (0.0387 mol) of β-ketol **2**[7] in 20.0 ml of anhydrous THF was added dropwise with stirring while the temperature was maintained at 0-5°C. After stirring for 15 min, 16.0 g (0.11 mol) of freshly distilled methyl iodide was added. After stirring for 10 min at 0°C, the mixture was allowed to warm to room temp. and stirred for 3 h. Water (100 ml) was then added with stirring, the organic layer was separated and the aqueous layer washed with two 100-ml portions of ether. The combined organic layer and washings were washed with three 50-ml portions of saturated

aqueous sodium chloride. The organic layer was dried over anhydrous magnesium sulfate, the solvent removed in vacuo, and the residue chromatographed on silica gel. Elution with 3 : 17 ethyl acetate-hexane gave 7.30 g (58%) of a 2 : 3 mixture (based on integration of the C-2 proton region of the ^{1}H NMR spectrum)[8,9] of acyclic unsaturated ketones **3a** and **3b** as a colorless oil. This oil showed only one spot (Rf = 0.69) by TLC using 1 : 9 ethyl acetate-hexane. The mixture could not be separated using other solvent combinations for development of the TLC plate. The mixture showed: IR(neat) 3095, 2980, 2940, 2885, 1712, 1655, 1592, 1480, 1460, 1445, 1390, 1370, 1125, 1090, 1030, 990, 895, 750, 705, and 690 cm^{-1}; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.35 (s, 3H), 1.41 (s, 3H), 1.73 (br s, 3H), 1.81 (br s, 3H), 2.05-2.21 (m, 2H), 2.68-2.93 (m, 2H), 2.95-3.07 (m, 1H), 4.80 (br s, 2H), 4.87-5.45 (m, 3H), 6.39 (dd J=17 Hz, 10 Hz, 0.4H), 6.76 (dd, J=17 Hz, 10 Hz, 0.6H), and 7.31 (s, 5H). Anal. Calc'd for $C_{21}H_{28}SO$: C, 76.78; H, 8.59; S, 9.76. Found: C, 76.66; H, 8.61; S, 9.81.

When a run was carried out under the same conditions as described above, except that the temperature was maintained at -78°C during the addition of the β- ketol **2**, integration of the ^{1}H NMR spectrum of the mixture in the region where the C-2 hydrogens absorb revealed that a *ca.* 1 : 9 mixture of **3a** and **3b** was produced.

Oxidation of Sulfides 3a and 3b to the Corresponding Sulfoxides (3c and 3d). A solution of 2.17 g (0.0126 mol) of 85% MCPBA in 125 ml of methylene chloride was added over 15 min to a stirred solution of 3.79 g (0.011 mol) of the 2 : 3 mixture of **3a** and **3b** in 100 ml of methylene chloride at -5°C and the solution was poured into 250 ml ether. The organic phase was washed with three 100-ml portions of 10% aqueous sodium bisulfite and dried over anhydrous magnesium sulfate. The solution was then filtered and the solvent removed in vacuo to give *ca.* 3.9 g of a crude mixture of sulfoxides **3c** and **3d**. The ^{1}H NMR spectrum of this mixture was essentially identical to that of **a mixture of 3a** and **3b**, with the exception of a very broad singlet at 7.56δ rather than 7.31 δ for the protons on the aromatic ring of the phenylsulfinyl group. This indicated that the E/Z diene ratio remained unchanged during the oxidation step.

Thermal Elimination of Phenylsulfinic Acid from the Mixture of Sulfoxides 3c and 3d at 78°C. The crude mixture of **3c** and **3d** (3.9 g, 0.011 mol) prepared in the previous step was dissolved in 40 ml dry benzene and the solution was heated at reflux for 1.0 h. After cooling to room temp., the mixture was poured into 100 ml of water and extracted with three 100 ml portions of ether. The combined organic extracts were dried over anhydrous magnesium sulfate and after filtration the solvent was removed under reduced pressure. The residue was subjected to flash column chromatography (silica gel, 1 : 19 ethyl acetate-hexane) to give 1.06 g (43%) of the Z diene derivative **4b** and 0.72 g (29%) of a mixture of diastereomeric octalones **5**. Analysis of this mixture by capillary column gas chromatography revealed that it contained three components in a *ca.* 15 : 7: 3 ratio.

Compound **4b** showed: IR(neat) 3110, 2995, 2975, 2890, 1695, 1665, 1465, 1450, 1385, 1090, 990, 940, 895, and 810 cm^{-1}; ^{1}H NMR (200 HMz) δ 1.70 (s, 3H, vinyl methyl), 1.80 (d, J=0.9 Hz, 3H vinyl methyl), 1.85 (br s, 3H, vinyl methyl), 1.92-2.40 (m, 2H), 2.74 (br s, 3H), 4.70 (br s, 1H), 4.75 (br s, 1H), 4.80-5.45 (m, 3H), 5.74 (br s, 1H), 5.90 (br s, 1H), 6.75 (dd, J=16 Hz, 10 Hz, 1H). Anal. Calc'd for $C_{15}H_{22}O$: C, 82.52; H, 10.16. Found: C, 82.38; H, 10.10.

The mixture of octalones was subjected to preparative gas chromatography. This allowed separation of the major component from a mixture of the middle and minor components. As described in the text, the major component was assigned structure **5a**. It showed: IR(neat) 2995, 2985, 1720, 1660, 1460, 1450, 1385, 1265, 1210,

1150, 1100, 1075, 1065, 1000, 915, 890, and 800 cm^{-1}; ^1H NMR (200 MHz) δ 1.10 (s, 3H, angular methyl group), 1.69 (d, J=1.25 Hz, 3H), 1.71-1.89 (m, 6H, including singlet at 1.78, 3H), 1.90-2.15 (m, 3H), 2.20-2.47 (m, 3H), 2.72 (t, J=12 Hz, 1H), 4.72 (br s, 2H), and 5.38 (br s, 1H); mass spectrum, *m/e* (70 eV): 218 (M^+), 107, 95, 93, and 91. Anal. Calc'd for $C_{15}H_{22}O$: C, 82.52; H, 10.16. Found: C, 82.53; H, 10.21.

As described in the text, the middle component was assigned the *cis*-octalone structure **5c** and the minor component was tentatively assigned the *trans*-octalone structure **5b**. The *ca.* 7 : 3 mixture of these components showed: IR(neat) same major absorptions as those listed for **5a**; ^1H NMR (200 MHz) δ 1.07 (s, 0.9H, angular methyl group of minor component), 1.16 (s, 2.1H, angular methyl group of the major component), 1.72 (br s, 3H, vinyl methyl), 1.73-1.79 (m, 5H including s at 1.76, 3H), 1.82-2.20 (m, 5H), 2.21-2.50 (m, 3H), 4.75 (m, 2H), 5.37(br s, 0.3H, vinyl hydrogen of minor component), 5.49 (br s, 0.7H, vinyl hydrogen of **5c**).

Reaction of the Z Diene Derivative 4b in Toluene at 150°C. A solution of 0.35 g (1.61 mmol) of compound **4b** in 35 ml of dry toluene containing a few mg of hydroquinone in a sealed heavy-walled glass tube was heated at 150°C for 50 h. After the mixture had been allowed to cool to room temp., it was poured into 100 ml of ether and the organic layer washed with two 50-ml portions of water. The organic layer was dried over anhydrous magnesium sulfate and after filtration, the solvent was removed under reduced pressure. The resulting oil was subjected to column chromatography (silica gel; 1 : 19 ethyl acetate-hexane) to yield 0.28 g (80%) of a mixture of octalones **5**. Analysis of this mixture by gas chromatography using a crosslinked dimethyl silicone capillary column revealed that it contained the *trans*-octalone **5a**, the *cis*-octalone **5c** and a minor component in a *ca.* 15 : 7: 3 ratio. The composition of this mixture was identical to that obtained from heating of the mixture of sulfoxides **3c** and **3d** in benzene where the E diene derivative **4a** underwent intromolecular Diels-Alder reaction as rapidly as it was formed.

Thermal Elimination of Phenylsulfinic Acid from the Mixture of Sulfoxides 3c and 3d at 150°C. The crude mixture of sulfoxides **3c** and **3d**, 2.75 g (0.008 mol), in 80 ml of dry toluene and 20 mg of hydroquinone was sealed in a thick-walled glass tube and heated at 150°C for 45 h. The mixture was allowed to cool to room temp., poured into 150 ml of diethyl ether, and the resulting solution extracted with two 50-ml portions of water. The organic layer was dried over anhydrous magnesium sulfate, the mixture filtered, and the solvent removed in vacuo to give 1.01 g (58%) of a mixture of octalones **5**. According to ^1H NMR and gas chromatographic analysis a mixture of octalones with an identical composition to the mixtures obtained upon heating the crude mixture of **3c** and **3d** in benzene for 1.0 h or upon heating the Z diene derivative **4b** in toluene at 150°C for 50 h, was obtained.

Wolff-Kishner Reduction of the Mixture of Octalones 5. To a solution of 1.8 g (8.26 mmol) of a 15 : 7 : 3 mixture of octalones **5** in 166 ml of triethylene glycol was added 6.94 g (0.066 mol) of hydrazine dihydrochloride and 18.39 g (0.545 mol) of 95% hydrazine. The mixture was then stirred and heated under nitrogen at 130°C for 2.5 h. Then, 10.2 g (0.18 mol) of potassium hydroxide was added and the temperature was increased to 210°C. The hydrazine-water azeotropic mixture was removed by distillation over 2.5 h while the temperature of the pot was maintained at 210°C. After being cooled to room temp., the reaction mixture was poured into 300 ml of ether and washed with two 100-ml portions of water. The organic layer was dried over anhydrous magnesium sulfate and, after filtration, the solvent was removed under reduced pressure. The residue was extracted with two 50-ml portions of hexane and after removal of the solvent 1.2 g (72%) of a mixture of octalins was obtained.

Analysis of the mixture by gas chromatography using a crosslinked dimethyl silicone capillary column showed that it contained a major component (45%), a middle component (35%), and four minor components none of which amounted to as much as 10% of the total mixture. The major component and the middle component were separated from the minor components by preparative gas chromatography using a 20% Silicone SE-30 on Chromosorb W packed column. The major component showed identical IR and ^{1}H NMR spectra to those previously published[12] for (-)-α-selinene (10), $[\alpha]_D^{25}$ -14.0° ($CHCl_3$, 0.5%) (lit.[12] -14.5° ($CHCl_3$, 1.0%); mass spectrum, *m/e* (70 eV): 204(M^+), 133, 107, 93, and 91; ^{13}C NMR δ 15.62 (angular methyl), 20.90, 21.17, 22.97, 26.81, 28.89, 32.28, 37.93, 40.22, 46.71, 46.78, 108.24, 120.90, 135.14, and 151.01.

The middle component was assigned the *cis*-octalin structure **11**. It showed: IR(neat) 2995, 2960, 2885, 1665, 1480, 1455, 1390, 990 and 810 cm^{-1}; ^{1}H NMR (200 MHz)δ 0.87 (s, 3H, angular methyl group), 1.33-1.72 (m, 16H including singlets at 1.66 (3H) and 1.72 (3H) for the vinyl methyl groups), 1.79-1.91 (m, 2H), 2.01-2.15 (m, 2H), 4.67 (br s, 2H, terminal methylene group), and 5.24 (b s, 1H, vinyl hydrogen); ^{13}C NMR δ 20.84, 22.63, 23.05, 26.11, 26.88, 27.16, 31.47, 34.68, 40.85, 45.81, 47.43, 108.08, 119.01, 136.99, and 150.86; high resolution mass spectrum, M^+ calc'd for $C_{15}H_{24}$ 204.188; found 204.185.

Preparation of β-Ketol (8). Following the procedure of Wasson and House[17] a 30% hydrogen peroxide solution (41.8 ml) was added slowly with vigorous stirring to a solution of 15.0 g (0.136 mol) of 2-methylcyclohex-2-enone[18] in 140 ml of methyl alcohol at 10°C. While the temperature was kept at or below 17°C, 11.36 ml of 6 N sodium hydroxide was added very slowly with stirring and the solution was stirred at room temp. overnight. The reaction mixture was poured into 100 ml of saturated aqueous sodium chloride and the mixture was extracted with four 50-ml portions of ether. The ethereal solution was dried over anhydrous magnesium sulfate and after filtration, the solvent was removed under reduced pressure. Distillation of the residue gave 9.70 g (56%) of 2-epoxy-2-methylcyclohexanone,[19] bp 70-72°C/7 mm; ^{1}H NMR (90 MHz) δ 1.40 (s, 3H), 1.65-2.69 (m, 6H), and 3.44 (m, 1H).

Thiophenol (8.46 g (0.077 mol)) was added dropwise with stirring to a solution of 9.67 g (0.076 mol) of 2-epoxy-2-methylcyclohexanone in 175 ml of dry acetonitrile. While the temperature was maintained at *ca.* 20°C, 7.77 g (0.077 mol) of triethylamine was added dropwise with vigorous stirring and stirring was continued for 12 h at room temp. The reaction mixture was poured into 100 ml of a saturated aqueous solution of sodium chloride and the resulting mixture was extracted with four 50-ml portions of methylene chloride. The combined extracts were dried over anhydrous magnesium sulfate, and after filtration, the solvent was removed under reduced pressure. The residue was subjected to chromatography on silica gel using 3 : 7 ethyl acetate-hexane as the eluting solvent to obtain 10.6 g (59%) of β-ketol **8** as an oil. This material showed: IR(neat) 3460, 3060, 2940, 2875, 1700, 1580, 1570, 1470, 1440, 1420, 1370, 1315, 1240, 1170, 1120, 1080, 1070, 960, 860, 750, 700, and 690 cm^{-1}; ^{1}H NMR (200 MHz) δ 1.24 (s, 3H), 1.85-2.47 (m, 6H), 3.21-3.37 (m, 1H), 4.16 (br s, 1H), 7.34 (br s, 5H). Anal. Calc'd for $C_{13}H_{16}O_2S$: C, 66.07; H, 6.82; S, 13.57. Found: C, 66.02; H, 6.87; S, 13.54.

Preparation of Mixture of E and Z Dienones 9a and 9b. To a solution of 7.35 g (0.0287 mol) of 1-methylallyldiphenylphosphine oxide **6** in 70 ml of anhydrous THF at -78°C was added 2.87 ml of a 10 M solution of n-butyllithium in hexanes. The mixture was stirred for 10 min and allowed to gradually warm up to -10°C. The temperature was then lowered to -78°C and 20 ml (0.115 mol) of HMPA was added. After stirring 15 min,

2.42 g (0.011 mol) of β-ketol **8** in 7.0 ml of anhydrous THF was added dropwise with stirring while the temperature was maintained at -78°C. After stirring 10 min, the mixture was allowed to warm up to 0°C and 6.25 g (0.044 mol) of freshly distilled methyl iodide was added. After stirring for 10 min at 0°C, the mixture was allowed to warm to room temperature and stirred for 3 h. Water (50 ml) was then added, the organic layer separated, and the aqueous layer extracted with two 50-ml portions of ether. The combined organic extracts were washed with three 50-ml portions of saturated aqueous sodium chloride. The organic layer was dried over anhydrous magnesium sulfate, the solvent removed in vacuo, and the residue chromatographed on silica gel. Elution with 3 : 17 ethyl acetate-hexane gave 1.51 g (51%) of a 3 : 1 mixture (based on integration of the C-2 proton region of the ^{1}H NMR spectrum)[8,9] of acyclic unsaturated ketones **9a** and **9b** as a colorless oil. The mixture showed: IR(neat) 3080, 3060, 2980, 2935, 2865, 1705, 1645, 1610, 1585, 1475, 1460, 1440, 1385, 1370, 1120, 1085, 1025, 990, 900, 810, 750, 705, and 695 cm^{-1}; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.41 (s, 6H), 1.66-1.83 (m, 10H, including s at 1.75, 3H), 2.15-2.25 (m, 2H), 2.78 (t, J=7.4 Hz, 2H), 4.92-5.49 (m, 3H), 6.38 (dd, J=17, 10 Hz, 0.75H), 6.78 (dd, J=17, 10 Hz, 0.25H). Anal. Calc'd for $C_{18}H_{24}OS$: C, 74.95; H, 8.39. Found: C, 74.86; H, 8.42.

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