Synthetic Studies on the Ochtodane Type Terpenes I. Stereoselective Construction of the Ochtodane Skeleton from Myrcene

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The ochtodane skeleton, the Carbon framework of 1,1-dimethyl-3-ethylcyclohexane (**1**) was constructed highly stereoselectively by the acid-catalyzed ($SnCl_4$ or CF_3CO_2H) cyclization of the terminally functionalized myrcene derivatives, the benzenesulfenyl chloride adduct (**7**), the terminal β-hydroxy sulfide (**8**) derived from **7**, and myrcene 6,7-epoxide (**10**). The stereoselectivity of the 3-exo-double bond in **1** formed concomitantly in the cyclization reaction was found to depend remarkably upon the reaction temperature and the 85—94% of *E*-stereoselectivity was attained at −78 °C. By the method, the ochtodane derivatives with the sulfur- or oxygen-functional groups on the C(6)-position were obtained. Synthetic applications of the ochtodane type compounds (**12**) and (**19**) to the aldehyde component (**4**) of the pheromone of the male boll weevils and to an ochtodane type terpene (**26**) isolated from the red alga *Ochtodes crockeri*, are reported.

In 1975 novel dihalogenated dimethylhexahydrobenzofurans including chondrocole A (**2**) were isolated by Moore from Hawaiian red alga *Chondrococcus hornemanni*.[1a] Recently, Fenical and coworkers have found a variety of polyhalogenated and/or oxygenated cyclic monoterpenes possessing the ring system of 1,1-dimethyl-3-ethylcyclohexane (**1**) in red seaweeds (Rhodophyta) of the genera *Chondrococcus* and *Ochtodes* (Rhizophyllidaceae),[1b] and they suggested the name "ochtodane" for the skeleton (**1**). They also reported that some of the ochtodane type monoterpenes appear to function as herbivore feeding deterrents in the marine environment and that a certain polyhalogenated compound of this class shows strong anti-bacterial activity. Interestingly, the less functionalized compounds (*Z*-**3**) and (*E*- and *Z*-**4**) with the carbon skeleton (**1**) already have been isolated and recognized by Tumlinson and coworkers in 1969 as the sex attractant and aggregating pheromonal components of the insect boll weevils *Anthonomus grandis* Boheman.[2a] These terpenes have been suggested to be biosynthesized from myrcene (**5**) directly or *via* the corresponding oxygenated or halogenated precursors in organisms.[1a,3] In the context, a unique sesquiterpene pleraplysillin-1 (**6**) isolated from a marine sponge *Pleraplysilla spinifera* may be classified as the higher homologue of the ochtodane type terpenes.[4]

Because of the practical interest in the agricultural purpose for extermination of noxious insects, a lot of synthetic efforts have focused on the pheromonal components (**3**) and (**4**).[2,5,6a] The biogenetic type cyclization of acyclic 1,5-dienes affording terpenoid-carbocycles was pioneered by Eschenmoser[7a] and by Stork,[7b] and has been extensively studied on not only the non-functionalized but also functionalized polyolefins.[7] In addition to the nonbiogenetic type synthetic route consisting of the two-carbons homologation of 3,3-dimethylcyclohexanone which in general appears non or less stereoselective concerning the geometry of the exocyclic double bond in (**3**) and (**4**),[2b,5] several routes utilizing the biogenetic type cyclization of acyclic monoterpenes including myrcene (**5**) have been reported: Acid-catalyzed cyclization of γ-geraniol,[6a] tricarbonyl myrcene iron,[6b] and 3,10-dihydromyrcene;[6c] and brominative cyclization of myrcene (**5**) using 2,4,4,6-tetrabromo-2,5-cyclohexadien-1-one.[6d] None of these precedents, however, has offered satisfactory stereoselectivities and requisite functionalizations for synthesis

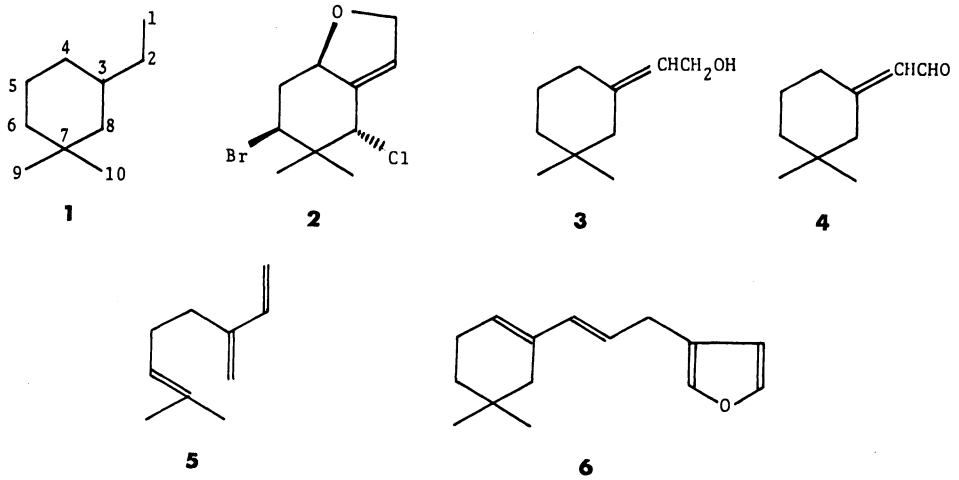


Chart 1.

of the highly functionalized ochtodane type terpenes. Here we disclose new biogenetic type and stereoselective cyclizations of myrcene (**5**) *via* the benzenesulfenyl chloride (PhSCl) adduct (**7**) or the epoxide (**10**) effectively affording the functionalized ochtodanes (**11—15, 17**) which are expected to be the promising intermediates for a variety of ochtodane type terpenes.[8]

Results and Discussion

In a general consideration concerning the possible acid- catalyzed cyclization of myrcene (**5**), the generated terminal tertiary cation (**i**) would cyclize to give the ochtodane type skeleton (**1**) and the other tertiary cation (**ii**), if generated, would form the cyclobutane framework (**iii**) found in glandisol which has been recognized to be the major pheromonal constituent of male boll weevils.[2] Wolinsky has examined the cyclization reaction of γ-geraniol (**iv**) and methyl γ-geranate (**v**) under acidic conditions and reported exclusive formation of the cyclohexane framework (**1**) so far.[6a] We also investigated in the preliminary experiments acid-catalyzed reactions of myrcene (**5**) itself under several conditions involving CF_3CO_2H (CH_2Cl_2/−20°C), $SnCl_4$ (CH_2Cl_2/0°C), 90% HCO_2H (reflux), and polyphosphoric acid (130°C), but the reactions produced complicated and intractable mixtures in all cases examined. Then we turned our attention to the examination of cyclization reaction of the terminally functionalized myrcene derivatives.

I) Acid-catalyzed Cyclization of Terminally Sulfur-substituted Myrcene Derivatives (Scheme 1). Mustafaeva reported that methyl geranate (**vi**) gave the cyclized product (**viii**) on treatment with PhSCl in the presence of $AgSbF_6$ in nitromethane by way of the *in situ* formed terminal adduct (**vii**)[9a] and Weiler also found that the PhSCl-adduct (**x**) of methyl 7-methyl-3-oxo-7-octenoate (**ix**) cyclized to give a cyclohexane derivative (**xi**) by refluxing with silica gel in CH_2Cl_2.[9b] Also we have observed the acid-catalyzed cyclization of terminally sulfur-functionalized geraniol and nerol derivatives (**xii, xiii**) affording the cyclohexane derivatives (**xiv, xv**).[10] Findings in the literatures[9] and our observations[10] prompted us to investigate the behaviors of the terminally sulfur-functionalized myrcene derivatives in the acid-catalyzed cyclization conditions.

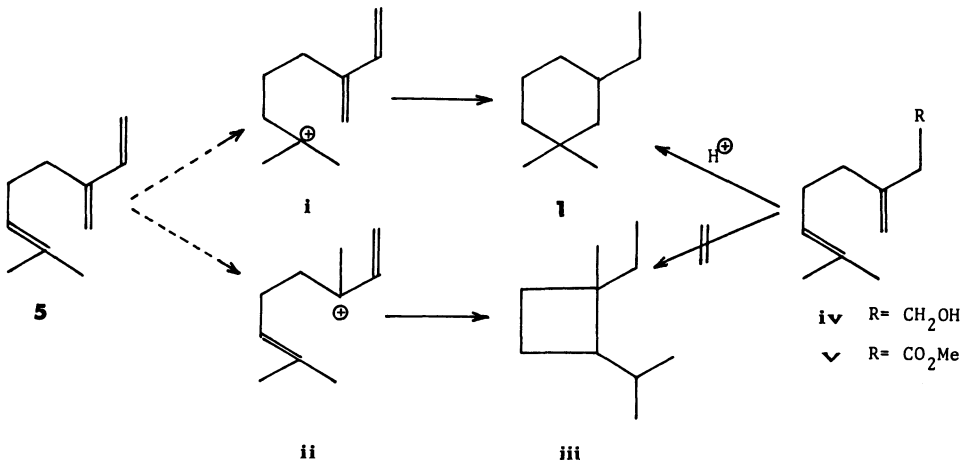


Chart 2.

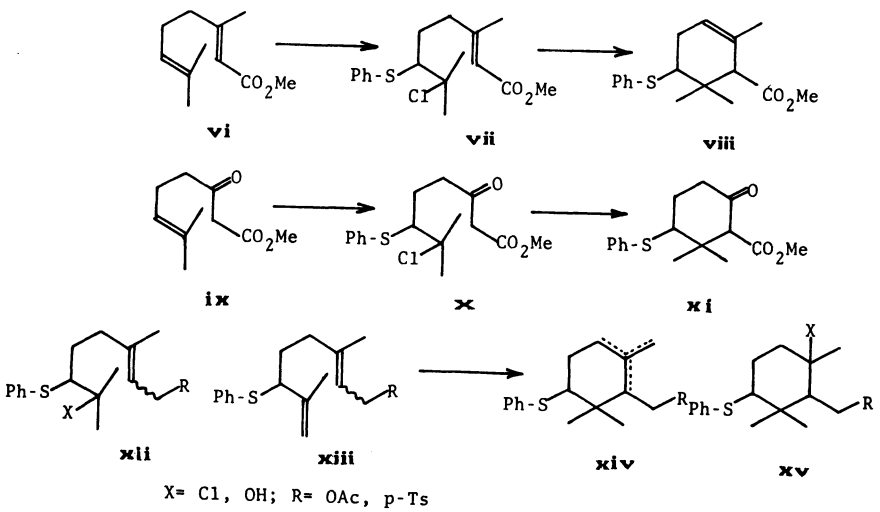
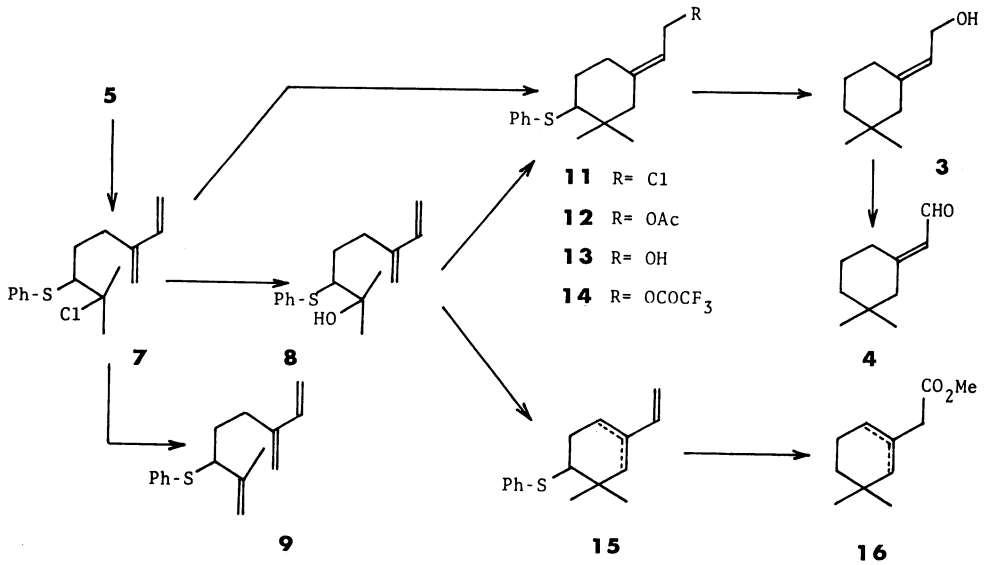


Chart 3.

The substrates, PhSCl-adduct (**7**), β-hydroxy sulfide (**8**), and terminal methallylic sulfide (**9**) was prepared from myrcene (**5**) by the method recently developed[11] for the terminal functionalzation of acyclic isoprenoids.

The crude adduct (**7**) was treated with 0.2equiv of $SnCl_4$ in CH_2Cl_2 at −20°C to produce expectingly the cyclized products (**11**) whose ^{1}H-NMR exhibited mainly sharp singlets at δ 0.69 and 1.16 assignable to the gem-dimethyl groups on the cyclohexane ring and a set of a doublet and a triplet respectively at δ 3.95 and 5.31 with the identical coupling constant (8.0Hz) assignable to the primary allylic chloride functionality. The crude product, without further purification, was converted to the corresponding acetate (**12**) by treatment with an excess amount of AcONa in *N,N*-dimethylformamide (DMF) at 60°C for 16h. Purification of the product by column chromatography on silica gel gave a stereoisomeric mixture of acetates (*E*-**12**) and (*Z*-**12**) in 58% overall yield from **5**. ^{1}H-NMR showed signals for one of the geminal methyl groups on the cyclohexane ring at δ 0.92 at a overlaped singlet and for the other one at δ 1.14 and 1.18 as the separate singlets in a ratio 75:25, the peaks which proved to be the diagnostic peaks representing the isomeric ratio. All of the other signals in ^{1}H-NMR, the molecular ion peak at *m/z* 304 in the mass spectrum, and the IR band at 1720cm^{-1} supported the structure of the acetate (**12**). The stereoisomeric ratio was finally determined by ^{1}H-NMR analysis of the aldehyde (**4**) derived from the acetate (**12**) by a sequence of reactions, *vide infra*. After alkaline hydrolysis of the acetate (**12**), desulfurization of the alcohol (**13**) obtained with Li in liquid NH_3 gave the sulfur-free alcohol (**3**) in 65% overall yield from **12**. Oxidation of the alcohol (**3**) with active MnO_2[12] led in 85% yield to the stereoisomeric mixture of α,β-unsaturated aldehydes (**4**), which are the components of the male boll weevil pheromone.[2] The *E/Z*-ratio of the aldehyde (**4**) was determined as 75:25 on the basis of its ^{1}H-NMR analysis: The diagnostic isolated allylic C(8)-methylene protons of each component were clearly observed as a couple of singlets at δ 2.05 (major) and 2.47 (minor) which had been assigned to that of the *E*- and *Z*-component respectively.[2,6a] On the detailed examination of the cyclization conditions, it was found that the stereoselectivity of the concomitant formation of the double bond in the present cyclization reaction is dependent upon the reaction temperature. Thus, cyclization of the adduct (**7**) using $SnCl_4$ (0.2equiv) at 0°C gave the *E/Z*-mixture of the acetate (**12**) in a ratio 59:41 after the subsequent acetoxylation of the crude chloride (**11**), and at −78°C yielded the *E/Z*-ratio of 85:15 contrastingly.

The cyclization reaction was investigated also on the β-hydroxy sulfide (**8**). On treatment of **8** with an excess amount of CF_3CO_2H in CH_2Cl_2 at −20°C, the cyclized trifluoroaceate (**14**) (62%) was obtained, whose isomeric ratio was tentatively estimated as 77:23 on the basis of ^{1}H-NMR analysis: The diagnostic signals of singlets indicating the isomeric ratio appeared at δ 1.16 (major) and 1.20 (minor) assignable to the one of the gem-dimethyl groups on the cyclohexane ring. The ratio was also verified by derivatization of **14** to the aldehyde (**4**) *via* hydrolysis of **14** leading to the alcohol (**13**). The analogous tendency of dependence of the stereoselectivity on the reaction temperature as described for the cyclization of the adduct (**7**) was observed and cyclization of **8** using CF_3CO_2H at 0°C gave a poor *E/Z*-ratio 64:36 of the trifluoroacetate (**14**). On the other hand, treatment of **8** with concd H_2SO_4 in Et_2O at room temperature afforded in this case a high yield (80%) of the regioisomeric cyclized diene mixture (**15**) in a ratio of 60:40 analyzed from its ^{1}H-NMR. The structure of **15** was confirmed by conversion to the regioisomeric mixture of the carboxylic ester

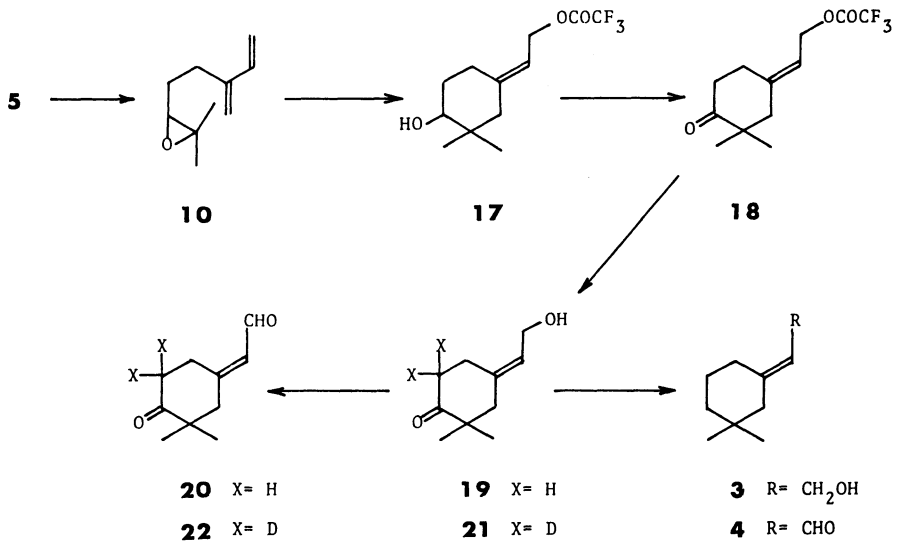


Scheme 1.

TABLE 1. ACID-CATALYZED CYCLIZATION OF THE TERMINALLY SULFUR-FUNCTIONALIZED MYRCENE DERIVATIVES (**7**) AND (**8**)

Substrate	Acid (mole equiv)	Reaction Conditions Solvent,	Temp	Time	Product (Ratio)	yield %	*E/Z*-ratio
7[a]	$SnCl_4$ (0.2)	CH_2Cl_2,	0°C,	30 min	**12**[b]	56	59:41
		CH_2Cl_2,	−20°C,	30 min	**12**[b]	58	75:25
		CH_2Cl_2,	−78°C,	30 min	**12**[b]	48	85:15
	$TiCl_4$ (0.3)	CH_2Cl_2,	−20°C,	30 min	**12**[b]	28	77:23
	CF_3CO_2H (excess)	CH_2Cl_2,	−20°C,	80 min	**11**+**14** (*ca.* 1:1)	55	—
8	$SnCl_4$ (1.0)	CH_2Cl_2,	0°C,	30 min	**12**[b]	54	50:50
	CF_3CO_2H (excess)	CH_2Cl_2,	0°C,	40 min	**14**	64	67:34
		CH_2Cl_2,	−20°C,	70 min	**14**	63	76:24
	H_2SO_4 (excess)	Et_2O,	15°C,	4 h	**15**	80	—

a) The crude adduct was used. b) The primary product (**11**) was not isolated and directly led to **12**.



Scheme 2.

(**16**), which have been reported by Wolinsky,[6a] by a sequence of reactions involving hydroboration, desulfurization, Jones oxidation, and then esterification.

On the substrate terminal methallylic sulfide (**9**), unfortunately, all the several attempted conditions (1.0equiv $SnCl_4/CH_2Cl_2/0$—15°C/1h; excess H_2SO_4/Et_2O/15°C/2h; excess CF_3CO_2H/CH_2Cl_2/15°C/1 h) were not effective for the expected cyclization and gave recovery of the starting material. Results of the cyclization reactions examined on the PhSCl-myrcene adduct (**7**) and the β-hydroxy sulfide (**8**) are summarized in Table 1.

II) Cyclization of Myrcene 6,7-Epoxide (Scheme 2). The terminal epoxide functionality has been utilized in the carbocyclization of acyclic polyisoprenoids as much more general and efficient initiator.[7d] To our knowledge, however, the acid-catalyzed carbocyclization of myrcene 6,7-epoxide (**10**) has never been precedented in the literature. In order to construct the functionalized ochtodane skeleton, cyclization of **10** appeared to be one of the attractive candidates. Thus, the epoxide (**10**) was stirred with an excess amount of CF_3CO_2H in CH_2Cl_2 at −20°C. The structural analysis of the product (**17**) obtained in 54% yield revealed that the desirable cyclization was realized. All the data including the IR band at 3400 and 1780 cm^{-1}, M^+ peak at *m/z* 266 in the mass spectrum, and ^{1}H-NMR signals for the gem-dimethyl groups at δ 0.81 and 0.91, the primary allylic trifluoroacetate system at δ 4.77 (2H, d) and 5.28 (1H, t), and the secondary hydroxyl functionality at δ 1.89 (OH) and 3.40 (1H, ABXq) fully supported the structure (**17**) although the stereoisomeric ratio could not be estimated. Oxidation of the alcohol (**17**) with pyridinium chlorochromate (PCC) afforded the ketone (**18**) in 87% yield. In ^{1}H-NMR the ketone (**18**) exhibited sharp singlets at δ 1.04 and 1.07 in a ratio of intensity 87:13 which was supposed to represent the *E/Z*-stereoisomeric ratio of **18**. Exact determination of the ratio was perfomed by the ^{1}H-NMR analysis of the keto aldehyde (**20**) and its dideuterated derivative (**22**) as described below. The compound (**18**) was subjected to alkaline hydrolysis to lead to the keto alcohol (**19**) (92%) which was oxidized to the keto aldehyde (**20**) in 78% yield with active MnO_2. Also in this compound, separate singlets were observed at δ 1.10 and 1.13 in a ratio 87:13 of intensity in ^{1}H-NMR. Correspondence of the ratio to the stereochemistry of the bouble bond in **20** was clearly attained by the ^{1}H-NMR analysis of the 5,5-dideuterio keto aldehyde (**22**) derived by the deuterium

Table 2. Cyclization of myrcene 6, 7-epoxide (**10**) using CF_3CO_2H[a)]

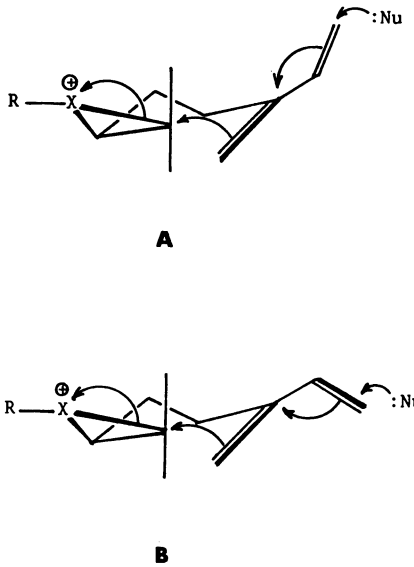
Reaction Temp (°C)	Product	Yield/%	*E*/*Z*-ratio
−5	**17**	53	83:17
−20	**17**	54	87:13
−78	**17**	43	94:6

a) The reaction was carried out in CH_2Cl_2 for 30 min by using 5.0 equiv of CF_3CO_2H.

exchange reaction[13)] of the keto alcohol (**19**) in MeOD with Na followed by oxidation of the 5,5-dideuterio keto alcohol (**21**) with active MnO_2. Generally, the γ-*cis*-methylene protons of α,β-unsaturated aldehydes and esters are known to appear in lower ^{1}H-NMR chemical shifts than the corresponding γ-*trans*-methylene protons by the paramagnetic deshielding effect of the spatially proximate carbonyl group.[2,6a,14)] Thus, the major pair of 2H-signals at δ 2.48 and 3.09 proved to be assigned to the C(8)- and C(4)-methylenes of the *E*-component (*E*-**22**) and the minor pair of 2H-signals at δ 2.67 and 2.86 to the C(4)- and C(8)-methylenes of the *Z*-component (*Z*-**22**), and therefore, the *E*/*Z*-ratio of **22** was determined clearly as 87:13, which was well consisted with the estimation on the trifluoroacetoxy ketone (**18**). The identical *E*/*Z*-ratio was indicated by ^{1}H-NMR analysis of the aldehyde (**4**) derived from the keto alcohol (**19**) *via* deoxygenation[15)] of the corresponding tosylhydrazone with $NaBH_4$ providing the allylic alcohol (**3**). The stereoselectivity in this cyclization also proved to be dependent upon the reaction temperature. As shown in Table 2, the lower temperature resulted in the formation of the *E*-component (*E*-**17**) in higher proportion.

We propose that the higher *E*-stereoselectivity in the trisubstituted double bond formation at the lower temperature in these cyclizations ascribes to the preferential tandem cyclization of the cation (**A**) with the *s*-*trans*-1,3-diene system and concerted formation of the exo-double bond to the reaction of the other cation (**B**) bearing the *s*-*cis*-1,3-diene system.

III) Synthesis of an Oxygenated Ochtodane Type Terpene, (±)-(2Z)-2,4-Ochtodadiene-1,6-diol (26) (Scheme 3). A simple and successful application of the functionalized ochtodanes (**12**) and (**19**) obtained was achieved in the stereoselective synthesis of a diol component (**26**) isolated from the red alga *Ochtodes crockeri*.[1b)] Oxidation of the 6-phenylthio derivative (**12**) (*E*:*Z*=85:15) with 30% H_2O_2 in AcOH followed by heating the intermediate sulfoxide in xylene gave the diene acetate (**23**) in 79% yield from **12**. The structure of the compound (**23**) was supported by the spectral analysis: The M^+ ion was observed at *m*/*z* 194 in the mass spectrum, and the signals of the newly formed C(4)-allylic methylene at δ 2.78 (major (*E*-**23**)) and 2.70 (minor (*Z*-**23**)) as broad singlets and of the C(5)- and C(6)-olefinic protons at δ 5.40—5.60 were detected in ^{1}H-NMR. On treatment of the diene (**23**) with an



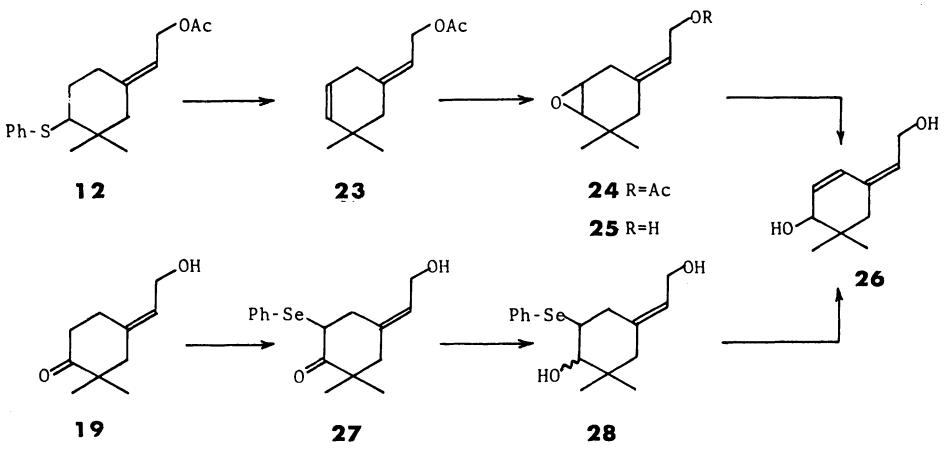
R= Ph, X= S
or
R= H, X= O

Chart 4.

equimolar amount of *m*-chloroperbenzoic acid in CH_2Cl_2 at −20°C, a selective epoxidation proceeded to lead in 59% yield the 5,6-epoxide (**24**), ^{1}H-NMR of which indicated that the allylic acetate system remained intact. Although the *E*- and *Z*-component of **24** were separable by column chromatography on silica gel, the tedious separation of the stereoisomers turned out to be not necessary for the synthesis of the target compound (**26**) because a unexpected kinetic stereoselection in the base promoted epoxide opening reaction of the epoxy alcohol (**25**) was observed. Thus, after alkaline hydrolysis of **24** (*E*:*Z*=15:85), the resulted epoxy alcohol (**25**) was treated with 2.5 equiv of lithium diisopropylamide (LDA) in THF at −78—−20°C for 2h to furnish the desired diol (**26**) as the single stereoisomer in 73% yield and a small amount of recovery (less than 10%) of the starting epoxy alcohol which was substantially enriched in the *E*-isomr.[16)] The dienediol (**26**) obtained was identified with the natural one[1b)] by spectral comparisons.

The dienediol (**26**) was also synthesized alternatively from the keto alcohol (**19**) *via* a tandem procedure of selenylation and elimination of selenenic acid.[17)] Selenylation of **19** was carried out with LDA and diphenyl diselenide to give the seleno keto alcohol (**27**) (70%). Reduction of **27** with $LiAlH_4$ afforded in 84% yield the selenodiol (**28**), which was treated with $NaIO_4$ in aqueous MeOH at room temperature providing the diol (**26**) in 61% yield.

In conclusion, we established a facile stereoselective method providing the ochtodane skeleton with the functional group on the C(6)-position. The compounds obtained are claimed to be the promising



Scheme 3.

intermediates for the synthesis of a variety of natural ochtodane type terpenes including pleraplysillin-1 (**6**),[4] a unique sesquiterpene which is recognized synthetically as the homologated ochtodane at the C(1)-position with furfuryl moiety. A successful application of the ochtodane derivative (**3**) obtained in this work to the synthesis of the sesquiterpene (**6**) will be reported in the following paper.[18]

Experimental

General. IR spectra were taken on a JASCO IRA-1 spectrometer in $CHCl_3$ solution and the absorption bands (ν_{max}) are reported in cm^{-1}. Mass spectra (MS) were obtained on a JMS-D300 instrument at an ionizing potential of 70eV and peaks are reported in *m/z* values with relative intensities (%) in parenthesis. ^{1}H-NMR spectra were recorded on a Hitachi R-20B spectrometer (60MHz) in CCl_4 solution, unless otherwise noted, with tetramethylsilane (TMS) as an internal standard and chemical shifts are reported in δ (ppm) relative to TMS and coupling constants (*J*) in hertz (Hz). All the solvents used in reactions were freshly distilled to remove moisture. Reactions were carried out usually under nitrogen unless otherwise noted. Reaction mixtures were usually worked up as follows: A mixture was extracted with Et_2O, washed with water or saturated brine and saturated aqueous $NaHCO_3$, if necessary, dried over anhydrous $MgSO_4$, concentrated *in vacuo* using a rotary evaporator at water aspirator pressure below room temperature, to give a crude product which was purified by column chromatography. Silica gel (Wakogel B-5F) and Wakogel C-200 were employed respectively for analytical thin-layer (TLC) and column chromatography using hexane-Et_2O solvent system.

Materials. Myrcene (**5**) was purchased from Tokyo Kasei (TCI). Benzenesulfenyl chloride (PhSCl) was freshly prepared according to the literature.[19] Myrcene 6,7-epoxide (**10**) was obtained by the reported method.[20] The terminal methallylic sulfide (**9**) was prepared according to our reported method.[11] The β-hydroxy sulfide, 2-methyl-6-methylene-3-phenylthio-7-octen-2-ol (**8**) was prepared as follows: To a solution of myrcene (**5**) (680mg, 5.0mmol) in CH_2Cl_2 (10ml) was added dropwise a solution of PhSCl (725mg, 5.0mmol) in CH_2Cl_2 (3.0ml) at −20°C. After being stirred for 10min, the mixture was concentrated *in vacuo* to give the crude adduct (**7**) (1.4g).[11] The adduct was dissolved in aq CH_3CN ($CH_3CN:H_2O$=5:1)(20ml) and stirred at room temperature for 20h.[11a] The mixture was worked up by the usual manner to give **8** (720mg, 55) as oil. Date for **8** follow: IR 3400, 1595, 1590; MS 262 (M^+, 71), 204 (43), 137 (40), 136 (100), 135 (74), 123 (93), 110 (57); NMR 1.16, 1.23 (each 3H, $(C\underline{H}_3)_2C(OH)$, 2.31 (1H, s, OH), 2.98 (1H, dd, *J*=11.0 and 3.0, CH(SPh)), 4.80—5.30 (4H, m, $2X=CH_2$), 6.03—6.54 (1H, dd, *J*=18.0 and 11.0, $C\underline{H}=CH_2$). The compound **8** was also obtained alternatively as follows: The crude adduct (**7**) prepared from **5** (5mmol) was stirred with AcONa (1.23g, 15mmol) in AcOH (20ml) at 20°C for 1h. Usual work-up of the mixture gave the corresponding acetate of the β-hydroxy sulfide (**8**) (990mg, 65%),[11b] which was hydrolyzed in EtOH (15ml) with 3% NaOH (15ml) at room temperature for 2h to give **8** (690 mg, 81%).

Acid-catalyzed Cyclization of the Terminally Sulfur-Functionalized Myrcence Derivatives (7) and (8). Cyclization of the Benzenesulfenyl Chloride-Myrcene Adduct (7) Catalyzed by $SnCl_4$. To a solution of the adduct (**7**) prepared from myrcene (**5**) (550mg, 4.0mmol) and PhSCl (600mg, 4.1mmol) in CH_2Cl_2 (12ml) at −20°C, was added dropwise over 5 min a solution of $SnCl_4$ (100μl, 0.85mmol) in CH_2Cl_2 (2.0ml) at −20°C. After being stirred for 30min at −20°C, the mixture was diluted with CH_2Cl_2, washed with successively with saturated $NaHCO_3$ and water, dried, and concentrated to give the crude 1-chloro-6-phenylthio-2-ochtodene (**11**) (1.09g) as oil: MS 282 ($(M+2)^+$, 30), 280 (M^+, 72), 245 (75), 170 (33), 135 (63), 110 (100); NMR 0.96 (3H, s, one of the CH_3 of $C(7)(CH_3)_2$),
1.16 (major) and 1.19 (minor) (overall 3H, singlets (75:25), the other one of $C(7)(CH_3)_2$), 3.95 (2H, d, *J*=8.0, $=CHC\underline{H}_2Cl$), 5.31 (1H, bt, *J*=8.0, $=C\underline{H}CH_2Cl$). The crude chloride (**11**), without further purification, was warmed with AcONa (550mg, 6.7mmol) in DMF (12ml) at 60°C for 16h. The reaction mixture was worked up by the usual manner to leave an oily product (1.02g). Purification of the product by column chromatography afforded the oily acetate, 1-acetoxy-6-phenylthio-2-ochtodene (**12**) (705mg, 58% from **5**). Data for **12** follow: IR 1720, 1580; MS 304 (M^+, 7), 244 (30), 135 (100), 134 (66); NMR 0.92 (3H, s, one of the CH_3 of $C(7)(CH_3)_2$), 1.14 (major) and 1.18 (minor) (overall 3H, singlets (75:25), the other one of $C(7)(CH_3)_2$), 1.95 (3H, s, CH_3CO_2), 2.83—3.10 (1H, dd, *J*=10.0 and 4.5, CH(SPh)), 4.46 (2H, d, *J*=7.5, $=CHC\underline{H}_2OAc$), 5.21 (1H, bt, *J*=7.5, $=C\underline{H}CH_2OAc$); Found: C, 70.75; H, 7.83%. Calcd for $C_{18}H_{24}O_2S$: C, 71.10; H, 7.95%. Cyclizations of **7** at 0°C and −78°C were

examined and the results are listed in Table 1.

Cyclization of 7 Catalyzed by $TiCl_4$. Cyclization of **7** was carried out at −20 °C in CH_2Cl_2 using 0.3 equiv of $TiCl_4$ by the same procedure as described above and the crude product was directly converted into the acetate (**12**) (28%, *E*:*Z*=77:23).

Cyclization of 7 Using CF_3CO_2H. A solution of the crude adduct (**7**) (140 mg) in CH_2Cl_2 (0.5 ml) was added dropwise over 5 min at −20 °C into a mixture of CH_2Cl_2 (3.0 ml) and CF_3CO_2H (0.5 ml, 6.5 mmol). After being stirred for 80 min, the mixture was poured into water and the product was extracted with CH_2Cl_2, washed successively with saturated $NaHCO_3$ and brine, dried, and concentrated. The crude product (137 mg) was purified by column chromatography to give the chloride (**11**) (35 mg, 25%) as the less polar fraction and the trifluoroacetate, 6-phenylthio-1-trifluoroacetoxy-2-ochtodene (**14**) (45 mg, 25%) as the more polar one, spectral data of which follow: IR 1780, 1660, 1580; MS 358 (M^+, 37), 248 (26), 135 (100), 134 (41); NMR 0.93 (3H, s, one of the CH_3 of C(7)(CH_3)$_2$), 1.16 (major) and 1.20 (minor) (overall 3H, s, the other one of C(7)(CH_3)$_2$), 2.87—3.10 (1H, dd, *J*=10.0 and 4.0, CH(SPh)), 4.77 (2H, d, *J*=7.5, =CHC$\underline{H}_2$OTfa), 5.32 (1H, bt, *J*=7.5, =C$\underline{H}$CH$_2$OTfa).

Acid-catalyzed Cyclization of the β-Hydroxy Sulfide (8) Using $SnCl_4$. To an ice-cold solution of **8** (260 mg, 1.0 mmol) in CH_2Cl_2 (5.0 ml), $SnCl_4$ (110 μl, 1.0 mmol) was added dropwise. Stirring was continued for 30 min at the temperature and the reaction was quenched by addition of water. The mixture was extracted with Et_2O and worked up by the usual manner providing the crude chloride (**11**) which was converted into the corresponding acetate (**12**) (164 mg, 54%). The *E*:*Z*-ratio (*ca.* 50:50) was determined by ^{1}H-NMR analysis of the diagnostic methyl signal at δ 1.14 and 1.18.

Cyclization of 8 Using CF_3CO_2H. To an ice-cold solution of **8** (130 mg, 0.5 mmol) in CH_2Cl_2 (10 ml), CF_3CO_2H (4.0 ml) was added dropwise over 25 min and stirring was continued for 15 min at 0 °C. The mixture was poured into water and the product was extracted with CH_2Cl_2. The organic layer was worked up by the usual manner to give the trifluoroacetate (**14**) (114 mg, 64%) as oil. The *E*:*Z*-ratio was determined as 64:36 by ^{1}H-NMR analysis of the diagnostic methyl signal at δ 1.16 and 1.20. Results of the reaction of **8** with CF_3CO_2H at −20 °C in CH_2Cl_2 are listed in Table 1.

Cyclization of 8 Using H_2SO_4. To a solution of **8** (2.62 g, 10 mmol) in Et_2O (110 ml) was added dropwise over 10 min a mixture of concd H_2SO_4 (3.7 ml) and Et_2O (25 ml) at room temperature and the mixture was stirred for 4 h. The usual work-up of the mixture followed by the isolation of the product afforded the isomeric mixture of diene (**15**) (1.95 g, 80%) as oil. Data for **15** follow: MS 244 (M^+, 56), 164 (45), 136 (59), 135 (100), 134 (95), 119 (57); NMR 1.02 and 1.16 (major pair of singlets of 60 intensity), 1.10 and 1.27 (minor pair of singlets of 40 intensity) (overall 6H, C(CH_3)$_2$), 3.00—3.23 (1H, dd, *J*=9.0 and 5.5, CH(SPh)), 4.75—5.65 (3H, m, C(1)H_2 and C(4)H or C(8)H), 6.02—6.50 (1H, dd, *J*=18.0 and 11.0, C(2)H); Found: C, 78.36; H, 8.41%. Calcd for $C_{16}H_{20}S$: C, 78.63; H, 8.25%.

6-Phenylthio-2-ochtoden-1-ol (13): A mixture of the acetate (**12**) (360 mg, 1.18 mmol), EtOH (5.0 ml), and 3% NaOH (5.0 ml) was stirred for 20 h at room temperature. After evaporation of EtOH, the residue was worked up by the usual manner to give a crude product (310 mg), which was purified by column chromatography yielding the alcohol (**13**) (276 mg, 89%) as oil. Data for **13** follow: IR 3320, 1660, 1580; MS 262 (M^+, 28), 244 (15), 152 (22), 135 (100), 134 (72); NMR 0.92 (3H, s, one of the CH_3 of C(7)(CH_3)$_2$), 1.14 (major) and 1.18 (minor) (overall 3H, s, the other one of C(7)(CH_3)$_2$), 1.62 (1H, s, OH), 2.00 (2H, s, C(8)H_2), 2.84—3.10 (1H, dd, *J*=10.5 and 4.5, CH(SPh)), 4.01 (2H, d, *J*=7.0, =CHC$\underline{H}_2$OH), 5.28 (1H, bt, *J*=7.0, =C$\underline{H}$CH$_2$OH); Found: C, 72.98; H, 8.45%. Calcd for $C_{16}H_{22}OS$: C, 73.23; H, 8.45%.

2-Ochtoden-1-ol (3): A solution of the alcohol (**13**) (102 mg, 0.4 mmol) in THF (0.5 ml) was added dropwise into a chilled (−78 °C) blue solution of Li (50 mg, 7 mgatm) in liq. NH_3 (*ca.* 10 ml) and the mixture was stirred for 30 min at the temperature. Then, reaction was quenched by introduction of gaseous butadiene followed by addition of MeOH (1.0 ml) to destroy the excess Li and the cold bath was removed to evaporate NH_3. The residue was worked up by the usual manner and the crude product was purified by column chromatography to give the alcohol (**3**) (44 mg, 73%) as oil. Data for **3** follow: IR 3400, 1660; MS 154 (M^+, 16%), 136 (58), 121 (45), 95 (57), 93 (100); NMR 0.87 (6H, s, C(CH_3)$_2$), 1.85 (major) and 1.92 (minor) (overall 2H, s, C(8)H_2), 2.43 (1H, s, OH), 3.97 (minor) and 4.02 (major) (overall 2H, d, *J*=7.0, =CHC$\underline{H}_2$OH), 5.24 (1H, d, *J*=7.0, =C$\underline{H}$CH$_2$OH).

2-Ochtoden-1-al (4): The aldehyde (**4**) was obtained in 85% yield from the alcohol (**3**) by oxidation with active MnO_2 in pentane according to the literature.[2] Data for **4** follow: IR 1680, 1640; NMR 0.93 (major) and 0.97 (minor) (overall 6H, s, C(CH_3)$_2$), 2.05 (major) and 2.47 (minor) (overall 2H, s, C(8)H_2), 2.65 (2H, bt, *J*=6.0, C(4)H_2), 5.67 (major) and 5.81 (minor) (overall 1H, d, *J*=8.5, =C$\underline{H}$CHO), 9.88 (minor) and 9.93 (major) (overall 1H, d, *J*=8.5, =CHC$\underline{H}$O).

Transformation of the Diene Mixture (15) to the Regioisomeric Mixture of Esters (16). To an ice-cold solution of **15** (245 mg, 1.0 mmol) in THF (5.0 ml), a 1/3 M (1 M=1 mol dm^{-3}) solution of BH_3–THF (3.0 ml) was added dropwise over 30 min and the mixture was stirred for 30 min at 0 °C. To the mixture was added dropwise 3 M NaOH (0.8 ml) and 30% H_2O_2 (0.8 ml) at 0 °C successively. After being stirred for 2 h at room temperature, the mixture was worked up to give the dihydro alcohol, 6-phenylthio-3-ochtoden-1-ol (140 mg, 62%) with a recovery of **15** (36 mg). Data for the dihydro alcohol follow: IR 3560, 3400, 1580; MS 262 (M^+, 61), 153 (100), 136 (70); NMR 0.98, 1.07 (major pair of singlets) and 1.03, 1.20 (minor pair of singlets) (overall 6H, C(CH_3)$_2$), 2.50 (1H, s, OH), 2.90—3.20 (1H, m, CH(SPh)), 3.53 (2H, t, *J*=7.0, C$\underline{H}_2$-OH), 5.20 (minor singlet of C(8)-olefinic H) and 5.34 (major broad singlet of C(4)-olefinic H); Found: C, 73.18; H, 8.57%. Calcd for $C_{16}H_{22}OS$: C, 73.23; H, 8.45%. The 6-phenylthio alcohol obtained was desulfurized to 3-ochtoden-1-ol in 81% yield by the same procedure described for **3**. Data for the alcohol follow: MS 154 (M^+, 96), 139 (99), 121 (98), 109 (100), 107 (70); NMR 0.89 (major) and 0.95 (minor) (overall 6H, s, C(CH_3)$_2$), 2.57 (1H, s, OH), 3.53 (2H, t, *J*=7.0, C$\underline{H}_2$OH), 5.15 (minor singlet of C(8)-olefinic H) and 5.39 (major broad singlet of C(4)-olefinic H). The alcohol (55 mg, 0.35 mmol) was dissolved in acetone (3.5 ml) and 15 drops of the Jones reagent prepared from CrO_3 (14 g), H_2O (100 ml), and concd H_2SO_4 (12 ml), was added to the ice-cold solution. The mixture was stirred for 2.5 h at 0 °C and then for 1 h at room temperature. Usual work-up of the mixture gave the crude carboxylic acid (55 mg) which was esterified with an ethereal solution of CH_2N_2 by the usual manner. Purification of the crude product by column chromatography provided the ester,

methyl 3-ochtoden-1-oate (**16**) (40mg, 62%). Spectral data of the ester were consistent with those reported by Wolinsky:[6a] IR 1740; NMR 0.91 (major) and 0.96 (minor) (overall 6H, s, $C(CH_3)_2$), 2.92 (2H, s, $=CCH_2CO_2$), 3.65 (3H, s, CO_2CH_3), 5.27 (minor singlet of C(8)-olefinic H) and 5.52 (major broad singlet of C(4)-olefinic H).

Cyclization of Myrcene 6,7-Epoxide (10). A solution of the epoxide (**10**) (300mg, 2.0mmol) in CH_2Cl_2 (1.0ml) was added dropwise into a mixture of CF_3CO_2H (0.8ml, 10mmol) and CH_2Cl_2 (8.0ml) at −20°C. The mixture was stirred for 20min at −20°C and then poured into water. Extraction of the mixture with CH_2Cl_2 followed by the usual work-up gave a crude product (427mg), which was purified by column chromatography to yield the hydroxy ester, 6-hydroxy-2-ochtodene-1-yl trifluoroacetate (**17**) (284mg, 54%). Data for **17** follow: IR 3400, 1780, 1660; MS 266 (M^+, 7), 248 (44), 152 (92), 135 (100), 134 (98), 119 (96); NMR 0.81, 0.91 (each 3H, s, $C(CH_3)_2$), 1.89 (1H, s, OH), 3.40 (1H, dd, J=8.0 and 4.0, $C\underline{H}(OH)$), 4.79 (2H, d, J=7.5, $=CHC\underline{H}_2OTfa$), 5.28 (1H, bt, J=7.5, $=C\underline{H}CH_2OTfa$); Found: C, 54.28; H, 6.53%. Calcd for $C_{12}H_{17}O_3F_3$: C, 54.13; H, 6.44%. Cyclization of **10** at −5°C and at −78°C was examined and the results are listed in Table 2, in which the *E*:*Z*-ratio was determined by ^{1}H-NMR analysis of the corresponding ketone (**18**) derived from **17**, *vide infra*.

6-Oxo-2-ochtoden-1-yl Trifluoroacetate (18): A solution of the alcohol (**17**) (80mg, 0.3mmol) in CH_2Cl_2 (0.5ml) was added dropwise into a solution of pyridinium chlorochromate (97mg) in CH_2Cl_2 (1.0ml) at room temperature and stirring was continued for 2h. To the mixture, Et_2O (5.0ml) was added and the insoluble materials were removed by filtration. The filtrate was concentrated and the residue was chromatographed to give the ketone (**18**) (69mg, 87%). Data for **18** follow: IR 1780, 1705; NMR 1.04 (major) and 1.07 (minor) (overall 6H, $C(CH_3)_2$), 2.33 (2H, s, $C(8)H_2$), 2.30—2.85 (4H, m, $COCH_2CH_2C=$), 4.89 (2H, d, J=7.5, $=CHC\underline{H}_2OTfa$), 5.53 (1H, bt, J=7.5, $=C\underline{H}CH_2OTfa$); Found: C, 54.82; H, 5.95%. Calcd for $C_{12}H_{15}O_3F_3$: C, 54.55; H, 5.72%.

1-Hydroxy-2-ochtoden-6-one (19): The trifluoroacetate (**18**) was hydrolyzed by treatment with a mixture of EtOH and 3% NaOH (1:1) at room temperature for 10min to give the oily keto alcohol (**19**) in 92% yield. Data for **19** follow: IR 3550, 3400, 1695; MS 168 (M^+, 15), 150 (100), 135 (17), 123 (32), 107 (72); NMR 1.03 (6H, s, $C(CH_3)_2$), 2.26 (2H, s, $C(8)H_2$), 2.35—2.80 (4H, m, $COCH_2CH_2C=$), 2.96 (1h, s, OH), 4.09 (2H, d, J=7.0, $=CHC\underline{H}_2OH$), 5.49 (1H, bt, J=7.0, $=C\underline{H}CH_2OH$); Found: C, 71.54; H, 9.85%. Calcd for $C_{10}H_{16}O_2$: C, 71.39; H, 9.59%.

5,5-Dideuterio-1-hydroxy-2-ochtoden-6-one (21): A solution of the keto alcohol (**19**) (30mg, 0.2mmol) in MeOD (0.5ml) was added into a solution of NaOMe in MeOD, prepared from Na (3mg) and MeOD (0.5ml), at room temperature and the mixture was stirred for 20h. After addition of D_2O (1.0ml), the mixture was extracted with Et_2O and worked up by the usual manner to give the 5,5-dideuterio keto alcohol (**21**) (21mg). Data for **21** follow: IR 3480, 1690; MS 170 (M^+, 15), 152 (100), 137 (26), 125 (40), 109 (98); NMR 1.03 (6H, s, $C(CH_3)_2$), 2.25 (2H, s, $C(8)H_2$), 2.50 (2H, s, $C(4)H_2$), 2.58 (1H, s, OH), 4.09 (2H, d, J=7.0, $=CHC\underline{H}_2OH$), 5.49 (1H, bt, J=7.0, $=C\underline{H}CH_2OH$).

6-Oxo-2-ochtodene-1-al (20): Active MnO_2 (1.0g) was added at 0°C into a stirred solution of the keto alcohol (**19**) (30mg, 0.2mmol) in $CHCl_3$ (10ml) and stirring was continued for 30min at the temperature. The mixture was filtered and the filtrate was purified by column chromatography to give the keto aldehyde (**20**) (28mg, 94%) as oil. Data for **20** follow: IR 1690, 1660; NMR 1.10 (major) and 1.13 (minor) (overall 6H, s, $C(CH_3)_2$), 2.39—2.70 (2H, m, $COC\underline{H}_2CH_2C=$), 2.48 (2H, d, J=2.0, $C(8)H_2$), 2.85—3.26 (2H, m, $C(4)H_2$), 5.89 (1H, dt, J=7.5 and 2.0, $=C\underline{H}CHO$), 9.93 (1H, d, J=7.5, $=CHC\underline{H}O$).

5,5-Dideuterio-6-oxo-2-ochtodene-1-al (22): The dideuterio keto aldehyde (**22**) was prepared from the dideuterio keto alcohol (**21**) by the same procedure described for **20**. Data for **22** follow: IR 1690, 1660; MS 168 (M^+, 56), 139 (97), 125 (100); NMR 1.10 (major) and 1.13 (minor) (overall 6H, s, $C(CH_3)_2$), 2.48 (major doublet (J=2.0)) and 2.67 (minor broad singlet) (overall 2H, $C(8)H_2$), 2.89 (minor) and 3.09 (major) (overall 2H, s, $C(4)H_2$), 5.89 (1H, dt, J=7.5 and 2.0, $=C\underline{H}CHO$), 9.93 (1H, d, J=7.5, $=CHC\underline{H}O$).

Deoxygenation of the Keto Alcohol (19) Providing the Alcohol (3). A mixture of the keto alcohol (**19**) (72mg, 0.4mmol) and *p*-toluenesulfonyl hydrazide (80mg, 0.4mmol) in MeOH (5.0ml) was heated under reflux for 4h. After cooling and addition of MeOH (4.0ml), $NaBH_4$ (325mg, 8.5mmol) was added portions to the mixture at 0°C, and the mixture was heated under reflux for 2h. The reaction mixture was concentrated and the residue was worked up by the usual manner to give a crude product (68mg). Purification of the product by column chromatography yielded the alcohol (**3**) (43mg, 65%). The alcohol exhibited identical spectra with those obtained from **13**.

Synthesis of (±)-(2Z)-2,4-Ochtodadiene-1,6-diol (26) Starting from the 6-Phenylthio Acetate (12). 1-Acetoxy-2,5-ochtodadiene (**23**): A mixture of the acetate (**12** *E*:*Z*=85:15) (1.3g, 4.3mmol), AcOH (15ml), and 30% H_2O_2 (460μl) was stirred for 20h at room temperature. The reaction mixture was poured into water and the mixture was extracted with CH_2Cl_2. The organic layer was worked up by the usual manner to give the crude sulfoxide (1.37g), which was, without further purification, heated under reflux with $NaHCO_3$ (720mg, 8.5mmol) in xylene (40ml) for 4h. The reaction mixture was diluted with Et_2O and worked up by the usual manner to give the oily diene acetate (**23**) (655mg, 79%). Data for **23** follow: IR 1725; MS 194 (M^+, 2), 134 (72), 119 (100); NMR 0.94 (major) and 0.98 (minor) (overall 6H, s, $C(CH_3)_2$), 1.95 (3H, s, CH_3CO_2), 2.08 (major) and 2.20 (minor) (overall 2H, s, $C(8)H_2$), 2.70 (minor) and 2.78 (major) (overall 2H, bs, $C(4)H_2$), 4.53 (2H, d, J=7.5, $=CHC\underline{H}_2OAc$), 5.33 (1H, bt, J=7.5, $=C\underline{H}CH_2OAc$), 5.40—5.60 (2H, m, CH=CH).

1-Acetoxy-5,6-epoxy-2-ochtodene (24): A solution of *m*-chloroperbenzoic acid (net 80%) (305mg, 1.4mmol) in CH_2Cl_2 (4.0ml) was added dropwise into a cold (−20°C) mixture of the diene acetate (**23** *E*:*Z*=85:15) (230mg, 1.2mmol) and $NaHCO_3$ (100mg, 1.2mmol) in CH_2Cl_2 (12ml) and the mixture was stirred for 3h at −20°C and then for 3.5h at 0°C. The reaction mixture was diluted with CH_2Cl_2 and worked up by the usual manner to give a crude product (260mg), which was purified by column chromatography to afford the oily epoxide (**24**) (135mg, 59%) with a small amount of the isomeric 1-acetoxy-2,3-epoxy-5-ochtodene (28mg). By careful column chromatography of the epoxide (**24**) on silica gel, the *E*- and *Z*-component were separable. The less polar and minor *E*-**24**: NMR ($CDCl_3$) 0.96, 1.12 (each 3H, s, $C(CH_3)_2$), 1.98 (2H, bs, $C(8)H_2$), 2.04 (3H, s, CH_3CO_2), 2.60 (2H, bd, J=3.0, $C(4)H_2$), 2.80 (1H, d, J=4.0, C(6)H), 3.23 (1H, m,

C(7)H), 4.54 (2H, d, J=7.0, =CHC$\underline{H}_2$OAc), 5.45 (1H, bt, J=7.0, =C$\underline{H}$CH$_2$OAc). The more polar and major *Z*-**24**: NMR ($CDCl_3$) 0.93, 1.10 (each 3H, s, C(CH_3)$_2$), 2.04 (3H, s, CH_3CO_2), 1.59, 2.25 (each 1H, d, J=13.0, C(8)H$_2$), 2.68 (2H, bs, C(4)H$_2$), 2.83 (1H, d, J=4.0, C(6)H), 3.23 (1H, br, C(5)H), 4.55 (2H, d, J=7.5, =CHC$\underline{H}_2$OAc), 5.28 (1H, bt, J=7.5, =C$\underline{H}$CH$_2$OAc); IR 1720; MS 210 (M^+, 2), 156 (76), 150 (100), 139 (91), 135 (92).

5,6-Epoxy-2-ochtoden-1-ol (25): A mixture of the epoxy acetate (**24**) (105mg) and 3% NaOH (4.0ml) in EtOH (4.0ml) was stirred for 1.5h at room temperature and the mixture was worked up by the usual manner to give the epoxy alcohol (**25**) (77mg, 92%). (*Z*)-**25**: IR 3560, 3400; MS 150 ($(M-18)^+$, 16), 135 (47), 121 (100), 107 (81); NMR ($CDCl_3$) 0.92, 1.06 (each 3H, s, C(CH_3)$_2$), 1.60, 2.21 (each 1H, d, J=14.0, C(8)H$_2$), 2.50 (1H, s, OH), 2.63 (2H, bs, C(4)H$_2$), 2.83 (1H, d, J=4.0, C(6)H), 3.21 (1H, m, C(5)H), 4.10 (2H, d, J=7.0, =CHC$\underline{H}_2$OH), 5.33 (1H, bt, J=7.0, =C$\underline{H}$CH$_2$OH). (*E*)-**25**: NMR ($CDCl_3$) 0.95, 1.10 (each 3H, s, C(CH_3)$_2$), 1.92 (2H, s, C(8)H$_2$), 2.42 (1H, s, OH), 2.54 (2H, bd, J=3.0, C(4)H$_2$), 2.78 (1H, d, J=4.0, C(6)H), 3.23 (1H, m, C(5)H), 4.08 (2H, d, J=7.0, =CHC$\underline{H}_2$OH), 5.48 (1H, bt, J=7.0, =C$\underline{H}$CH$_2$OH).

(±)-(2Z)-2,4-Ochtodadiene-1,6-diol (26): To a solution of lithium diisopropylamide (LDA) in THF, prepared from diisopropylamine (110μl), 1.6M solution of *n*-BuLi–hexane (0.53ml) in THF (1.5ml) at −20°C, was added dropwise a solution of the epoxy alcohol (**25** *E*:*Z*=15:85) (50mg, 0.3mmol) in THF (0.5ml) at −78°C under argon. The mixture was stirred for 40min under gradual warming up to −20°C, and then for 1h at −20°C. Reaction was quenched by addition of water and the mixture was worked up by the usual manner. Purification of the crude product by column chromatography afforded the oily diene diol (**26**) (38mg, 73%) with a small amount of recovery of starting material (**25**) (8mg) which proved to change in the *E*:*Z*-proportion to the ratio *E*:*Z*=70:30 from ^{1}H-NMR analysis. Spectral data of **26** obtained were consistent with those reported for the natural one:[1b] IR 3500, 3300, 1650, 1600; MS 168 (M^+, 15), 150 (45), 135 (68), 107 (100); NMR ($CDCl_3$) 0.87, 0.97 (each 3H, s, C(CH_3)$_2$), 1.73 (2H, s, 2×OH), 2.13 (2H, s, C(8)H$_2$), 3.95 (2H, d, J=3.0, C$\underline{H}$(OH)), 4.25 (2H, d, J=7.0, =CHC$\underline{H}_2$OH), 5.47 (1H, bt, J=7.0, =C$\underline{H}$CH$_2$OH), 5.75 (1H, dd, J=10.0 and 3.0, C(5)H), 6.43 (1H, d, J=10.0, C(4)H).

*Synthesis of **26** Starting from the Keto Alcohol (**19**). 1-Hydroxy-5-Phenylseleno-2-ochtoden-6-one (**27**)*: To a solution of LDA in THF, prepared from diisopropylamine (170μl) and 1.6M solution of *n*-BuLi–hexane (0.75ml) in THF (1.5ml), was added dropwise a solution of the keto alcohol (**19**) (84mg, 0.5mmol) in THF (0.5ml) at −78°C under argon and the mixture was stirred for 15min at −78°C and then for 45min at −20°C. After warming up of the mixture to 0°C, a solution of diphenyl diselenide (156mg, 0.5mmol) in THF (0.5ml) was added rapidly into the mixture. Stirring was continued for 1h at room temperature and the mixture was poured into water. The mixture was extracted with Et_2O and worked up by the usual manner to give a crude product (229mg). Purification of the product by column chromatography afforded the oily seleno keto alcohol (**27**) (89mg, 70%) and a recovery of the strating material **19** (18mg). Data for **27** follow: IR 3560, 3400, 1690, 1580; MS 324 (M^+, 28), 167 (100), 149 (65); NMR 1.08, 1.16 (each 3H, s, C(CH_3)$_2$), 2.30 (1H, s, OH), 2.10—3.20 (4H, m, C(4)H$_2$ and C(8)H$_2$), 3.97 (2H, d, J=7.0, =CHC$\underline{H}_2$-OH), 3.90—4.15 (1H, m, CH(SePh)), 5.52 (1H, bt, J=7.0, =C$\underline{H}$CH$_2$OH); Found: C, 59.32; H, 6.37%. Calcd for $C_{16}H_{20}O_2Se$: C, 59.44; H, 6.24%.

5-Phenylseleno-2-ochtodene-1,6-diol (28): A solution of the seleno keto alcohol (**27**) (90mg, 0.3mmol) in Et_2O (2.0ml) was added dropwise into a chilled auspension of $LiAlH_4$ (22mg, 0.6mmol) in Et_2O (1.0ml) at −20°C and the mixture was stirred for 2h at −20°C and then for 1h at room temperature. Reaction was quenched by addition of wet Et_2O and the mixture was decanted to remove inorganic substances. The organic layer was worked up by the usual manner. Purification of the product by column chromatography provide the oily seleno diol (**28**) (76mg, 84%) as a diastereoisomeric mixture. Data for **28** follow: IR 3560, 3450, 1660, 1580; NMR 0.78, 0.80, 0.98, 1.02 (each 3/2H, s, C(CH_3)$_2$), 1.30—3.80 (8H, m, 2×OH, C$\underline{H}$(OH), CH(SePh), C(4)H$_2$, and C(8)H$_2$), 4.02 (2H, bd, J=7.0, =CHC$\underline{H}_2$OH), 5.30 (1H, bt, J=7.0, =C$\underline{H}$CH$_2$OH).

(±)-(2Z)-2,4-Ochtodadiene-1,6-diol (26): To a solution of the seleno diol (**28**) (50mg, 0.15mmol) in MeOH (2.0ml) and water (0.75ml) was added $NaIO_4$ (65mg, 0.3mmol) in portions at 0°C. The mixture was stirred for 15min at 0°C and then for 7h at room temperature. After addition of 5% $NaHCO_3$ (5.0ml), the mixture was extracted with CH_2Cl_2 and worked up by the usual manner. Purification of the product by column chromatography gave the oily diene diol (**26**) (16mg, 61%), which showed identical apectral data with those obtained from **25**.

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