Biogenetic Model Reactions of Epoxygermacrones

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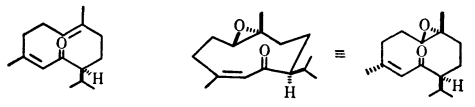
From a biogenetic point of view, acid- or base-catalyzed cyclizations of epoxygermacrones (**2**, **23**, and **33**) were carried out. In most cases, the stereospecific cyclizations of these epoxygermacrones took place to give many compounds with an 11-oxabicyclo[5.3.1]undecane system, cadinane-type, selinane-type or guaiane-type compounds depending on the kinds of reagents and solvents. The formation process of each cyclization product will be discussed in detail.

In the preceding paper,[1] we described the regio- and stereo-specific cyclizations of the germacrones in detail. Our interests are also focused on the biogenetic model reactions of the epoxygermacrones. In the present paper, we describe the acid-catalyzed cyclizations of three different kinds of epoxygermacrones leading to the formation of various cyclization products depending on the kinds of reagents and solvents. In addition, the base-catalyzed cyclizations of these epoxygermacrones are also discussed.

When treated with *m*-chloroperbenzoic acid (1.06 equiv.) (0 °C, 20 h), isoacoragermacrone (**1**)[2] was readily converted into the expected monoepoxide (**2**) (mp 55 °C; $C_{15}H_{24}O_2$; λ_{max} 243 nm), in a quantitative yield, which has an *E*-epoxide ring at the position corresponding to the isolated trisubstituted double bond of the original ketone (**1**). Epoxyisoacoragermacrone (**2**) thus obtained is used for the biogentic model reactions, as follows.[3]

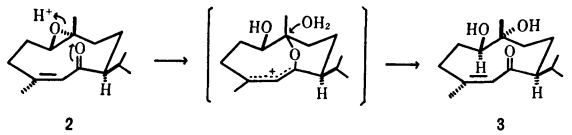


1 2

Fig. 1.

Acid-catalyzed Cyclizations of Epoxyisoacoragermacrone (2)

On treatment with 80% aq. HCOOH (−20 °C, 10 min), **2** was converted into a dihydroxy ketone (**3**) and a *cis*-selinate-type compound (**4**) in 47.5 and 34.2% yields, respectively. Of these two products, the structure of the former is based on its spectral data, which indicate the presence of a $-CH_2CH(OH)-\overset{Me}{\overset{|}{C}}(OH)-$grouping [$\nu_{max}$ 3400 br. cm^{-1}; δ 1.22 (3H, s) and 3.48 (1H, dd, J=4.0 and 6.0 Hz) ppm] in addition to the original α,β-unsaturated carbonyl system [ν_{max} 1685 and 1645 cm^{-1}; λ_{max} 238 nm (ε, 4200); δ 1.87 (3H, d, J=1.2 Hz) and 5.98 (1H, br.s) ppm]. The configuration of the tertiary OH group remains unsolved from the spectral data of **3**. However, this hydroxyl group must be in an α-configuration from a stereochemical aspect, as shown in Scheme 1.



2 3

Scheme 1. Formation process of the dihydroxy compound (**3**).

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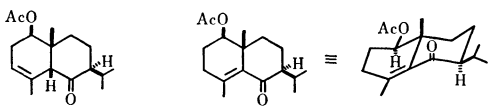
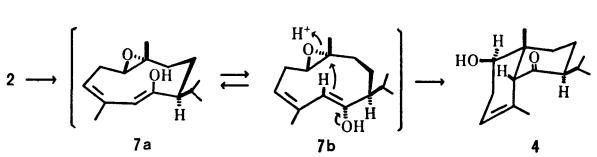


5 6

Fig. 2.

The structure of the *cis*-selinane-type compound (**4**) is unambiguously determined by its spectral data and the chemical evidences, as follows. The cyclization product (**4**) as a colorless liquid [$C_{15}H_{24}O_2$ (*m/e* 236 (M^+))] has each one of OH and CO groups (ν_{max} 3430 br. and 1705 cm^{-1}), the NMR spectrum of which indicates the presence of a $MeC(=CH-)$ grouping [δ 1.58 (3H, br.s) and 5.44 (1H, br.s) ppm] in addition to a tertiary methyl group [δ 1.02 (3H, s) ppm]. Acetylation of **4** with Ac_2O-pyridine (room temp, overnight) afforded the corresponding acetoxy compound (**5**) ($C_{17}H_{26}O_3$; ν_{max} 1740 and 1710 cm^{-1}). In its NMR spectrum, the triplet at δ 3.53 (1H, J=5.0 Hz) ppm in **4** is observed at δ 4.80 (1H, t, J=4.5 Hz) ppm. The remaining signals are nearly identical in both compounds. Furthermore, the ORD curve of **5** showed a negative Cotton effect ($[\phi]^T_{318nm}$ $-72°\times10^2$; $[\phi]^P_{276nm}+63°\times10^2$; $A=-135$), strongly suggesting that the acetate **5** is a *cis*-selinane-type ketone. This is further confirmed by the following acid-catalyzed isomerization with 100% HCOOH: when treated with 100% HCOOH under reflux for 10 h, the acetoxy compound **5** was converted into a fully substituted α,β-unsaturated ketone (**6**) [$C_{17}H_{26}O_3$; λ_{max} 246 nm (ε, 4800); δ 1.71 (3H, br.s) ppm], whose ORD curve has a strong positive peak ($[\phi]^P_{264nm}+150°\times10^2$) as seen in that of cholest-4-en-6-one. Finally, in comparison of the NMR spectra between **5** and **6**, the coupling constant for the proton attached to the carbon atom bearing the acetoxyl group in the latter [δ 4.85 (1H, dd, J=6.2 and 9.0 Hz) ppm] is different from that of **5** [δ 4.80 (1H, t, J=4.5 Hz) ppm]. Clearly, the configuration of the acetoxyl group should be axial in **5** and equatorial in **6**. Therefore, the stereostructures of the cyclization product and the acid-isomerization compound can be represented by **4**



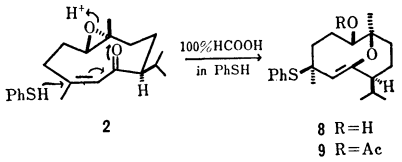
7a 7b 4

Scheme 2. Possible pathway from epoxyisoacoragermacrone (**2**) to the *cis*-selinane-type compound (**4**).

and **6**, respectively. In the above acid-catalyzed cyclization, a conjugated dienol (**7**) is a possible intermediate as shown is Scheme 2, and the stereochemistry of the cyclization product (**4**) must be led by the more favorable conformation of **7b** than that of **7a**.

We further examined the acid-catalyzed reactions of epoxyisoacoragermacrone (**2**) using 100% HCOOH in thiophenol. When treated with 100% HCOOH in thiophenol (room temp, 40 min) instead of 80% aq. HCOOH, epoxyisoacoragermacrone (**2**) was readily converted into an enol ether (**8**) with an 11-oxabicyclo-[5.3.1]undec-1-ene system, in a 65.5% yield. This compound has two tertiary methyl groups (δ 1.21 and 1.35 ppm) and the original isopropyl group (δ 0.86 and 0.88 ppm). Furthermore, the compound **8** has a PhS group [δ 7.30 (5H, complex) ppm] as well as an enol ether system (–Ċ–CH=Ċ–O–) [ν_{max} 1665 cm^{-1} and δ 4.75 (1H, s) ppm], in addition to one secondary OH group [ν_{max} 3420 br. cm^{-1} and δ 4.25 (1H, br.t, $J\simeq$6.0 Hz) ppm] which can be easily acetylated with Ac_2O–pyridine to give the corresponding acetate [**9**; ν_{max} 1735 cm^{-1} and δ 5.57 (1H, br.t, $J\simeq$6.8 Hz) ppm].

In the above reaction, the regio- and stereospecific cyclization of **2** takes place in a concerted mechanism, leading to the formation of **8**, as shown in Scheme 3.

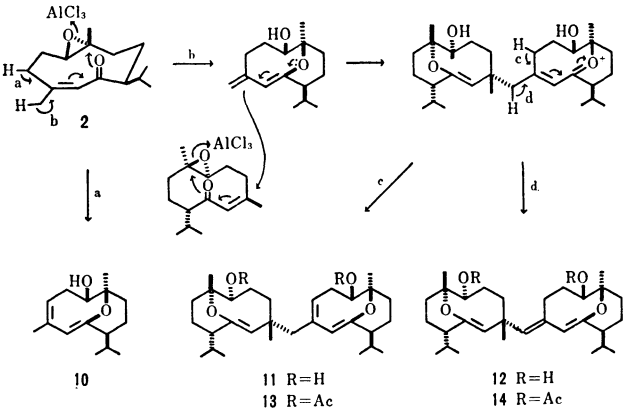


Scheme 3. Reaction of epoxyisoacoragermacrone (**2**) with 100% HCOOH in thiophenol.

Furthermore, the acid-catalyzed cyclization of **2** with $AlCl_3$ in absolute ether were carried out at −18 °C for 20 min to give three products **10**, **11**, and **12** in 18, 47, and 33% yields, respectively.

The compound **10** is a colorless liquid [$C_{15}H_{24}O_2$ (*m/e* 236 (M^+))] with a conjugated diene system [–CH_2–CH=C(Me)–CH=Ċ–O–] [ν_{max} 1650 cm^{-1}; λ_{max} 243 nm (ε, 7500); δ 1.79 (3H, br.s), 5.15 (1H, s) and 5.34 (1H, t, J=6.8 Hz) ppm]. The presence of each one of secondary OH and tertiary methyl groups is also confirmed by its spectral data [ν_{max} 3430 br. cm^{-1} and δ 3.45 (1H, dd, J=5.8 and 3.7 Hz) ppm; δ 1.35 (3H, s) ppm]. Other two compounds (**11**, mp 159.5—160.5 °C; **12**, mp 143.5—144.5 °C) with the same molecular formula ($C_{30}H_{48}O_4$) are dimeric and regarded as double bond isomers to each other, which are converted into the corresponding acetates **13** and **14**, respectively, on acetylation with Ac_2O–pyridine. The results indicate the presence of two secondary OH groups. The structures of these two dimeric compounds are also determined on the basis of their spectral data, as follows. Similarly, the NMR spectra of both compounds have three methyl singlets in addition to signals due to two isopropyl groups. However, a remarkable difference is seen in the NMR signals assigned to three olefinic protons: **11** has two singlets at δ 4.46 and 5.15 ppm and one triplet at δ 5.41 (1H, t, J=7.0 Hz) ppm, while **12** has three singlets at δ 4.79, 5.33 and 5.96 ppm. In addition, the UV spectra of these two compounds show different chromophores [**11**, λ_{max} 247 nm (ε, 6670); **12**, λ_{max} 254 nm (ε, 22400)]. From these data, the structures **11** and **12** should be given to the two dimeric compounds with mp 159.5—160.5 and 143.5—144.5 °C, respectively.

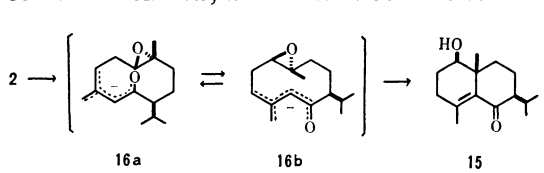
In the case of $AlCl_3$, clearly, the acid-catalyzed reaction of **2** must be initiated by cleavage of the epoxide ring with $AlCl_3$ followed by simultaneous participation of the carbonyl group, as shown in Scheme 4.



Scheme 4. Reaction of epoxyisoacoragermacrone (**2**) with $AlCl_3$.

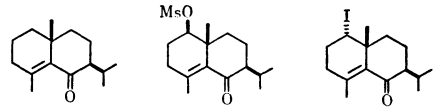
Base-catalyzed Cyclizations of Epoxyisoacoragermacrone (2). In the case of the acid-catalyzed cyclization with $AlCl_3$, the driving force of the intramolecular cyclization at the initial step may be attributable to the epoxide ring openning. In contrast, the different results were obtained in the case of the base-catalyzed reactions, as described below.

When treated with *t*-BuOK in *t*-BuOH (1.1 equiv.) under a nitrogen atmosphere (room temp, 2 h), the epoxide (**2**) was readily converted into an α,β-unsaturated ketone **15** ($C_{15}H_{24}O_2$) in a 75% yield, which was further converted into the known acetate (**6**) on acetylation with Ac_2O–pyridine. In the above cyclization using *t*-BuOK, **16** is regarded as a possible intermediate, and the stereochemistry of **15** must be led by the corresponding conformation **16b**, as shown in Scheme 5.



Scheme 5. Chemical conversion of **2** into the selinane-type compound **15**.

In connection with acolamone and isoacolamone,[2,4] both of which are included in the plant together with acoragermacrone,[2] this α,β-unsaturated ketone (**15**) was converted into the thermal isomerization product (**17**) of acolamone, in three steps, as follows. On treatment with mesyl chloride–pyridine (room temp, 2 h), the compound **15** was converted into the corresponding mesylate (**18**) [δ 3.07 (3H, s) and 4.21 (1H, t, J=7.5 Hz) ppm] in an almost quantitative yield. Further treatment of **18** with NaI in methyl ethyl ketone (under



17 18 19

Fig. 3.

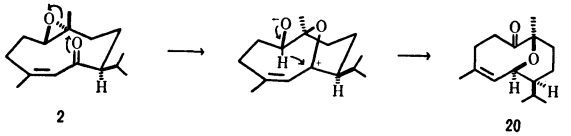
reflux, 15 h) afforded the corresponding iodide (**19**) [δ 4.31 (1H, dd, J=7.0 and 2.0 Hz) ppm]. which was directly reduced with n-Bu_3SnH in toluene (under reflux, 4 h) to give the compound **17**.

We further examined the base-catalyzed cyclization of **2** using basic alumina, as follows. Epoxyisoacoragermacrone (**2**) was directly absorbed on basic alumina (150—250 mesh), and then eluted with hexane–benzene (1 : 3) to give an isomer **20** with a CO group (ν_{max} 1715 cm^{-1}), in a 34% yield. Further elution with ether gave a fairly unstable isomer **21**, which has a secondary OH group [ν_{max} 3400 br. cm^{-1}; δ 4.32 (1H, dd, J=6.5 and 9.5 Hz) ppm], in a 46% yield. The structures of these two reaction products are based on their spectral data and the chemical evidences, as follows. Either of these compounds has a tertiary methyl group (δ 1.18 ppm in **20**; δ 1.27 ppm in **21**) in addition to the original isopropyl group. However, the former has a MeC=CH–CH–O– grouping [δ 1.86 (3H, br.s), 3.77 (1H, br.d, J=7.9 Hz) and 5.88 (1H, br.d, J=7.9 Hz) ppm], which was hydrogenated over 5% Pd–C to give the corresponding dihydro-compound **22**, mp 37—40 °C; $C_{15}H_{26}O_2$: δ 1.08 (3H, d, J=6.5 Hz) and 3.27 (1H, m) ppm. On the other hand, the alcohol **21** has a conjugated diene system (CH_2=C–CH=C–O–), as judged by its IR, UV and NMR spectra: ν_{max} 1650 and 1600 cm^{-1}; λ_{max} 240 nm (ε, 16160); δ 4.67 (1H, br.m), 4.79 (1H, d, J=2.4 Hz) and 5.58 (1H, s) ppm.

21 22

Fig. 4.

In the above reaction using basic alumina, an intramolecular H^- transfer may take place, leading to the formation of **20**, as shown in Scheme 6.



2 20

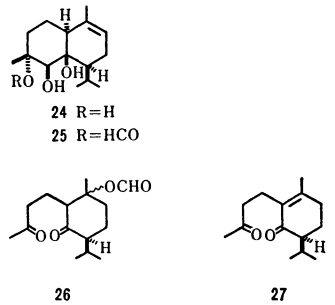
Scheme 6. Formation process of the keto compound (**20**).

In the next experiment, epoxidation of isoacoragermacrone (**1**) was carried out using 30% H_2O_2–5% NaOH aq. solution (room temp, overnight) to afford an epoxygermacrone (**23**) in a 92% yield (mp 85.5—86 °C; $C_{15}H_{24}O_2$; ν_{max} 1720 cm^{-1}: δ 1.42 (3H, s) and 3.43 (1H, s) ppm], which has an epoxide ring[5] at the position corresponding to the conjugated double bond of isoacoragermacrone (**1**). This epoxide (**23**) was also submitted to the biogenetic model reactions,[6] as seen in the case of **2**.

23

Fig. 5.

Acid-catalyzed Cyclizations of the Epoxygermacrone (23). This epoxide (**23**) is quite stable to 80% aq. AcOH at room temperature. However, when heated at 60 °C for 3 h, **23** was converted into a cadinane-type compound **24** [mp 195 °C (decomp.); $C_{15}H_{26}O_3$] in a 48% yield. This cyclization product **24** was also obtained in an 8% yield together with the corresponding formate (**25**) [ν_{max} 1720 cm^{-1}; δ 8.04 (1H, s) ppm] in a 15% yield, on treatment of **23** with 80% aq. HCOOH (room temp, 10 min). The latter (**25**) was readily converted into **24** on hydrolysis with 10% methanolic KOH. The structure of the cadinate-type compound (**24**) was determined by its spectral data [ν_{max} 3400 br. cm^{-1}; δ 1.32 (3H, s), 1.73 (3H, br.s), 3.90 (1H, br.s) and 5.64 (1H, m) ppm] and the following chemical evidence. When treated with $NaIO_4$ in aq. MeOH (room temp, overnight), the compound **24** was converted into a diketone (**26**) as a colorless liquid [ν_{max} 1720 br. cm^{-1} and no OH band; δ 1.26 (3H, s), 2.12 (3H, s) and 8.00 (1H, s) ppm]. This oxidation product (**26**) was further treated with NaOMe–MeOH (under reflux, 4 h) to give an α,β-unsaturated ketone in a high yield, whose structure was proved to be **27** by its spectral data: ν_{max} 1710 and 1660 cm^{-1}; λ_{max} 243 nm (ε, 10300); δ (C_6D_6) 1.56 (3H, s), 1.72 (3H, s), 2.30 (2H, t, J=7.8 Hz), and 2.65 (2H, t, J=7.8 Hz) ppm.



24 R=H
25 R=HCO

26 27

Fig. 6.

Probably, the intramolecular cyclization of **23** takes place after cleavage of the epoxide ring. From a biogenetic point of view, the formation of the trisubstituted olefins (**24** and **25**) is interesting. The further acid-catalyzed cyclization of the epoxygermacrone (**23**) was carried out using $AlCl_3$ in absolute ether.

On treatment with $AlCl_3$ in absolute ether (0 °C, 10 min), the epoxide (**23**) afforded a mixture of several compounds, from which two cyclization products **28** and **29** were isolated in 27 and 32% yields, respectively. The former (**28**) is an aldehyde [$C_{15}H_{24}O_2$ (m/e 236 (M^+)); ν_{max} 2700 and 1720 cm^{-1}; δ 9.75 (1H, s) ppm], and has no OH group. The NMR spectrum of **28** indicates the presence of two tertiary methyl groups (δ 1.25 and 1.52 ppm)[7] in addition to the original isopropyl group. On reduction with $LiAlH_4$ in THF (room temp, overnight). the aldehyde (**28**) was converted

into the corresponding alcohol **30** ($C_{15}H_{26}O_2$) which was a tertiary hydroxymethyl group [ν_{max} 3400 cm^{-1}: δ 3.56 (1H, d, J=12 Hz) and 3.76 (1H, d, J=12 Hz) ppm]. It was acetylated with Ac_2O–pyridine to give an acetate (**31**); $C_{17}H_{28}O_3$; ν_{max} 1740 cm^{-1}; δ 2.07 (3H, s) and 4.10 (2H, br.s) ppm. This alcohol was easily reconverted into the original aldehyde (**28**), in a 52% yield, on oxidation with Jones reagent (room temp, 1.5 h). From the above spectral and chemical data, the structure of the aldehyde can be represented by **28**.

The compound **29** has the same molecular formula as that of **28**. However, the former has no CO group, but instead a hydroxyl group (ν_{max} 3560 cm^{-1}). As described above, the aldehyde (**28**) has two tertiary methyl groups, while **29** has one methyl group [δ 1.67 (3H, s) ppm] and one exocyclic double bond [δ 4.66 (1H, br.s) and 4.86 (1H, br.s) ppm] that can be converted into a secondary methyl group on catalytic hydrogenation leading to the formation of the corresponding dihydro-compound (**32**); $C_{15}H_{26}O_2$ [m/e 238 (M^+)]; δ 1.10 (3H, d, J=8 Hz) and 2.85 (1H, m) ppm. From a structural point of view, particularly, it is important that the NMR spectra of **29** and **32** both have the two sharp doublets with a geminal coupling constant (J= 12 Hz) which can be assigned to the isolated methylene group (δ 2.90 and 3.31 ppm in **29**; δ 2.86 and 3.18 ppm in **32**). From these data, the structure of the alcohol may be represented by **29**.

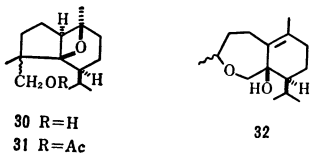
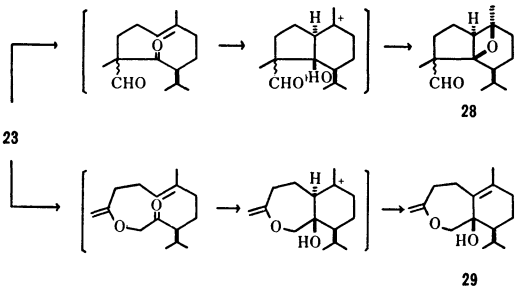


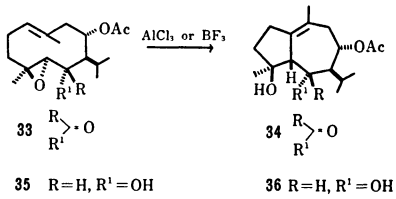
Fig. 7.

In the above reaction of the epoxygermacrone (**23**) with $AlCl_3$, these two cyclization compounds **28** and **29** may be produced according to the following pathways, as shown in Scheme 7.



Scheme 7. Possible pathways from **23** to the compounds **28** and **29**.

Finally, we used the oxidation product (**33**) of shiromodiolmonoacetate[8] as an (*E*,*E*)-epoxygermacrone, as will be described below. This epoxide (**33**) is also stable to 80% aq. AcOH at room temperature, as seen in the case of the (*Z*,*E*)-epoxygermacrone (**23**). However, when heated at 80 °C for 4 h, the epoxide (**33**) was converted into a mixture of many products, from which a guaiane-type compound (**34**) was isolated in a low yield (*ca.* 15%). The structure of **34** is based on its mass, IR and NMR spectra: $C_{17}H_{26}O_4$ [m/e 276 (M^+−18) and 234 (M^+−60)]; ν_{max} 3420, 1735 and 1710 cm^{-1}; δ 0.98 (3H, d, J=7 Hz) and 1.05 (3H, d, J= 7 Hz) [*i*-Pr], 1.36 (3H, s) [Me–C(OH)–], 1.71 (3H, br.s) [Me–C=C–], 2.05 (3H, s) and 5.30 (1H, m) [AcO–CH–] and 3.54 (1H, br.s) ppm [=C–CH–C=O]. This guaiane-type compound (**34**) was also produced in a 40% yield on treatment with $AlCl_3$ in absolute ether (−5 °C, 15 min). These results are quite similar to that of shiromodiol monoacetate (**35**), the acid-catalysed cyclization of which has afforded the corresponding guaiane-type compound (**36**).[8]



Scheme 8. Acid-catalyzed cyclization of the (*E*,*E*)-epoxygermacrone or -germacrene.

Experimental

All the mps are uncorrected. GLC were recorded on a Shimadzu GC-1C gas chromatograph with a flame-ionizer detector (stationary phase: 5% PEG 20 M on Celite 545 (100 mesh); column (ϕ 3 mm × 1.5 m (stainless steel)] temp: 90 °C; carrier gas: nitrogen (85 ml/min); inlet pressure: 1.2 Kg/cm^2], unless otherwise stated. IR spectra were recorded on a Hitachi-215 spectrophotometer. UV spectra were taken on a Hitachi-124 spectrophotometer, using MeOH as the solvent. NMR spectra were recorded on a Varian Associate A-60 (60 MHz), a Nihondenshi JNM-C60H (60 MHz) or JNM-PS 100 (100 MHz), using $CDCl_3$ as the solvent, unless otherwise stated. The chemical shifts are given in ppm relative to the internal TMS, and only prominent signals are cited (d, doublet; m, multiplet; q, quartet; s, singlet; t, triplet). Mass spectra were obtained on a Hitachi RMU-6D mass spectrometer operating at an ionization energy of 70 eV. ORD curves were recorded on a JASCO ORD/UV spectrophotometer, using MeOH as the solvent. Preparative TLC were carried out on Kieselgel PF_{254} (E. Merck, A. G.), unless otherwise stated.

Epoxidation of Isoacoragermacrone (1) with m-*Chloroperbenzoic Acid.* To a solution of **1** (1.10 g) in ether (40 ml) was added, with stirring, *m*-chloroperbenzoic acid (920 mg) at 0 °C. The resulting solution was further stirred at 0 °C for 20 h, and then washed successively with sat. Na_2SO_3, sat. $NaHCO_3$ and sat. NaCl aq. solutions, and then dried over anhydrous Na_2SO_4. Removal of the solvent afforded a crystalline solid of **2** (1.18 g), which was recrystallized from hexane to give colorless columns; mp 55 °C; ν_{max} (KBr) 1675 and 1620 cm^{-1}; λ_{max} 243 nm (ε, 6400); δ 0.93 (3H, d, J=6.5 Hz), 0.97 (3H, d, J=6.5 Hz), 1.21 (3H, s), 1.91 (3H, d, J=1.3 Hz) and 6.20 (1H, br.s) ppm; m/e 236 (M^+), 193 and 175 (Found: C, 76.30; H, 10.47%. Calcd for $C_{15}H_{24}O_2$: C, 76.22; H, 10.24%).

Reaction of 2 with 80% aq. HCOOH. The compound **2** (260 mg) was dissolved, with stirring, in 80% aq. HCOOH (8 ml) at −18——20 °C. The resulting solution was further stirred at the same temperature for 10 min, and then diluted with ice water (*ca.* 40 ml) and extracted with CH_2Cl_2. The extract was washed successively with a sat. $NaHCO_3$ aq. solu-

tion and water, and then dried over anhydrous $MgSO_4$. Evaporation of the solvent under reduced pressure afforded crude crystals, which were washed with ether to leave insoluble crystals of the dihydroxy ketone **3** (94 mg). The ethereal solution was concentrated under reduced pressure to give an oil, which was separated by preparative TLC using alumina [GF_{254} (type E), E. Merck, A. G.] and hexane–ether (2: 1) to give **3** (39 mg) and the *cis*-selinane-type compound **4** (89 mg).

3: mp 155—157 °C (from Et_2O–MeOH); ν_{max} (KBr) 3400 br., 1680 and 1645 cm^{-1}; λ_{max} 238 nm (ε, 4200); δ 0.93 (6H, d, J=6.5 Hz), 1.22 (3H, s), 1.87 (3H, d, J=1.2 Hz), 3.48 (1H, dd, J=4.0 and 6.0 Hz), and 5.98 (1H, br. s) ppm; *m/e* 236 (M^+-18) and 210 (Found: C, 70.81; H, 10.57%. Calcd for $C_{15}H_{26}O_3$: C, 70.83; H, 10.30%).

4 as a colorless viscous liquid: ν_{max} (film) 3430 br. and 1705 cm^{-1}; δ 0.91 (6H, d, J=5.0 Hz), 1.02 (3H, s), 1.58 (3H, br. s), 3.53 (1H, t, J=5.0 Hz), and 5.44 (1H, br. s) ppm; *m/e* 236 (M^+) and 193 (Found: *m/e* 236.17726. Calcd for $C_{15}H_{24}O_2$: *m/e* 236.17762).

Acetylation of the Selinane-type Compound (4). A solution of **4** (85 mg) in Ac_2O–pyridine (2: 5) (7 ml) was stirred at room temperature overnight, and then poured into a cooled 5% HCl aq. solution, and extracted with ether. The ethereal extract was washed successively with water, 5% $NaHCO_3$ aq. solution and water, and then dried over anhydrous $MgSO_4$. Removal of the solvent under reduced pressure gave an oil, which was purified by preparative TLC using alumina [GF_{254} (type E), E. Merck, A. G.] and hexane–ether (5: 1) to afford **5** (53 mg) as a colorless viscous liquid; ν_{max} (film) 1740, 1710, and 1245 cm^{-1}; δ 0.90 (6H, d, J=5.1 Hz), 0.98 (3H, s), 1.62 (3H, br. s), 2.03 (3H, s), 4.80 (1H, t, J=4.5 Hz), and 5.45 (1H, br. s) ppm; *m/e* 278 (M^+), 237, and 219 (Found: 278.18864. Calcd for $C_{17}H_{26}O_3$: *m/e* 278.18818).

Acid-catalyzed Isomerization of the Acetate (5) with 100% HCOOH. A solution of **5** (50 mg) in 100% HCOOH (3 ml) was refluxed for 10 h under a nitrogen atmosphere, and then slowly poured into a sat. $NaHCO_3$ aq. solution and extracted with ether. The ethereal extract was washed with water, and then dried over anhydrous $MgSO_4$. Removal of the solvent left a brown oil (42 mg) which was separated by preparative TLC using alumina [GF_{254} (type E), E. Merck, A. G.] and hexane–ether (4: 1) to give the starting material **5** (8 mg) and the α,β-unsaturated ketone **6** (10 mg) as a colorless viscous liquid; ν_{max} (film) 1745, 1690, 1630, and 1250 cm^{-1}; λ_{max} 246 nm (ε, 4800); δ 0.89 (3H, d, J=6.8 Hz), 0.95 (3H, d, J=6.8 Hz), 1.01 (3H, s), 1.71 (3H, br. s), 2.07 (3H, s). and 4.85 (1H, dd, J=6.2 and 9.0 Hz) ppm; *m/e* 278 (M^+), 237, and 219 (Found: *m/e* 278.18670. Calcd for $C_{17}H_{26}O_3$: *m/e* 278.18818).

Acid-catalyzed Reaction of Epoxyisoacoragermacrone (2) in Thiophenol. To a solution of **2** (160 mg) in thiophenol (2 ml) was added, with stirring, 5 drops of 100% HCOOH at room temperature. The resulting solution was further stirred at room temperature, and then diluted with a cooled 10% NaOH aq. solution (20 ml) and extracted with ether. The ethereal extract was washed successively with a cooled 10% NaOH aq. solution and water, and then dried over anhydrous $MgSO_4$. Removal of the solvent afforded an almost colorless liquid, which was purified by preparative TLC using alumina [GF_{254} (type E), E. Merck, A. G.] and hexane–benzene (1: 1) to give the enol ether **8** (165 mg) as a colorless viscous liquid; ν_{max} (film) 3420 br., 3060 sh., 3950, 1665, 1580, 745, and 690 cm^{-1}: δ 0.86 (3H, d, J=6.0 Hz), 0.88 (3H, d, J=6.0 Hz), 1.21 (3H, s), 1.35 (3H, s), 1.49 (1H, s, OH), 4.25 (1H, br. t, $J\simeq$6.0 Hz), 4.75 (1H, s), and 7.30 (5H, complex) ppm; *m/e* 236 (M^+—PhSH) and 221 (Found: *m/e* 236.17410. Calcd for $C_{15}H_{24}O_2$ ($C_{21}H_{30}O_2S-C_6H_6S$)*: *m/e* 236.17762).

Acetylation of 8 with Ac_2O–Pyridine. To a solution of **8** (60 mg) in pyridine (2 ml) was added Ac_2O (0.5 ml) at 0 °C. The solution was allowed to stand at the same temperature overnight, and then diluted with ice water (*ca.* 20 ml) and extracted with ether. The ethereal extract was washed successively with a cooled 10% HCl aq. solution and water, and then dried over anhydrous $MgSO_4$. Removal of the solvent under reduced pressure left a colorless viscous liquid (61 mg) in an almost pure state, which was further purified by preparative TLC using benzene to give **9** (58 mg) as a colorless viscous liquid; ν_{max} (film) 3050, 1735, 1665, 1580, 1240, 745, and 690 cm^{-1}; δ 0.87 (6H, d, J=6.0 Hz), 1.25 (3H, s), 1.37 (3H, s), 2.00 (3H, s), 4.82 (1H, s), 5.57 (1H, br. t, $J\simeq$6.8 Hz), and 7.35 (5H, complex) ppm; *m/e* 279 (M^+-109) and 278 (M^+-110) (Found: *m/e* 279.19579. Calcd for $C_{17}H_{27}O_3$ ($C_{23}H_{32}O_3S-C_6H_5S$)*: *m/e* 279.19601).

Reaction of 2 with $AlCl_3$ in Absolute Ether. To a solution of **2** (325 mg) in absolute ether (15 ml) was added, with stirring, a solution of $AlCl_3$ (200 mg) in absolute ether (4 ml) at −18 °C. The solution was further stirred at −18—−20 °C for 20 min, and then diluted with ether saturated with water. The ethereal solution was washed successively with a sat. potassium sodium tartarate aq. solution and a sat. NaCl aq. solution, and then dried over anhydrous Na_2SO_4. Removal of the solvent afforded a residue, which was dissolved in ether (2 ml). Precipitated colorless crystals of the dimer **11** (95 mg) was collected by filtration. The filtrate was concentrated, and the residue was subjected to preparative TLC using alumina [GF_{254} (type E), E. Merck, A. G.] and hexane–ether (1: 1) giving two fractions. From the less polar fraction, the compound **10** (60 mg) was isolated as a colorless liquid; ν_{max} (film) 3430 br., 3030 sh. and 1650 cm^{-1}; λ_{max} 243 nm (ε, 7500); δ 0.95 (6H, d, J=5.3 Hz), 1.35 (3H, s), 1.79 (3H, br. s), 1.69 (1H, s, OH), 3.45 (1H, dd, J=3.7 and 5.8 Hz), 5.15 (1H, s) and 5.34 (1H, t, J=6.8 Hz) ppm: *m/e* 236 (M^+ for $C_{15}H_{24}O_2$), 221, 218, and 175. Elemental analysis of **10** was not carried out because of its instability, but its structure was supported by the above-mentioned physical data.

From the more polar fraction, a colorless oil was obtained, which was further separated by preparative TLC using $CHCl_3$–MeOH (100: 5) to give two dimers **11** (59 mg) and **12** (107 mg). Their physical data are shown below.

11: mp 159.5—160.5 °C (from hexane–ether); ν_{max} (KBr) 3450 br., 1680 and 1660 cm^{-1}; λ_{max} 247 and 205 nm (ε, 6670 and 13680, respectively); δ 0.96 (12H, complex), 1.01 (3H, s), 1.28 (3H, s), 1.39 (3H, s), 3.21 (1H, t, J=4.0 Hz), 3.93 (1H, t, J=6.1 Hz), 4.46 (1H, s), 5.15 (1H, s), and 5.41 (1H, t, J=7.0 Hz) ppm; *m/e* 472 (M^+), 238, 237, 236, and 219 (Found: *m/e* 472.35658. Calcd for $C_{30}H_{48}O_4$: *m/e* 472.35524).

12: mp 143.5—144.5 °C (from hexane–ether); ν_{max} (KBr) 3390 br., 1680, and 1650 cm^{-1}; λ_{max} 254 and 203 nm (ε, 22400 and 11800, respectively); δ 0.90 (12H, complex), 1.08 (3H, s), 1.18 (3H, s), 1.23 (3H, s), 1.51 (2H, s, OH), 3.32 (1H, br. m), 4.26 (2H, br. m), 4.79 (1H, s), 5.33 (1H, s), and 5.96 (1H, s) ppm; *m/e* 472 (M^+), 238, 237, 236, and 219 (Found: *m/e* 472.35714. Calcd for $C_{30}H_{48}O_4$: *m/e* 472.35524).

Acetylation of the Dimer 11. To a solution of **11** (100 mg) in pyridine (5 ml) was added Ac_2O (2 ml) at 0 °C. The resulting solution was further stirred at 0 °C overnight, and then poured into ice water and extracted with ether. The ethereal extract was washed successively with a cooled 5% HCl aq. solution, a cooled sat. $NaHCO_3$ aq. solution, and water, and then dried over anhydrous Na_2SO_4. After evaporation of the solvent, the residue was purified by preparative TLC using

* No molecular ion peak was observed.

alumina [GF_{254} (type E), E. Merck, A. G.] and benzene to give **13** (62 mg) as a colorless viscous liquid; ν_{max} (film) 3040, 1740, 1670, and 1250 cm^{-1}; δ 0.83—1.00 (12H, complex), 1.00 (3H, s), 1.27 (6H, s), 2.00 (3H, s), 2.06 (3H, s), 4.64 (1H, s), 5.26 (1H, s), and 4.87—5.74 (3H, complex) ppm (Found: *m/e* 556.37888. Calcd for $C_{34}H_{52}O_6$: *m/e* 556.37637).

Acetylation of the Dimer **12**. To a solution of **12** (90 mg) in pyridine (5 ml) was added Ac_2O (2 ml) at 0 °C. The resulting solution was stirred at 0 °C overnight, and then treated according to the same procedure as that for **11** to give an oil, which was purified by preparative TLC using AcOEt–benzene (1: 10) to give **14** (61 mg) as a colorless viscous liquid; ν_{max} (film) 1740, 1680, 1650, and 1240 cm^{-1}; δ 0.90 (12H, complex), 1.11 (3H, s), 1.22 (3H, s), 1.28 (3H, s), 2.02 (6H, s), 3.48 (1H, m), 4.87 (1H, s), 5.38 (1H, s), 5.31—5.67 (2H, m), and 5.99 (1H, s) ppm (Found: *m/e* 556.37982. Calcd for $C_{34}H_{52}O_6$: *m/e* 556.37637).

Base-catalyzed Reaction of **2** *with* t-*BuOK*. To a solution of potassium metal (25 mg) in *t*-BuOH (4 ml) was added, with stirring, a solution of **2** (137 mg) in *t*-BuOH (1 ml) at 25 °C under a nitrogen atmosphere. The solution was further stirred at 25 °C for 2 h, and then diluted with water (10 ml) and extracted with ether. The ethereal extract was washed with water, and then dried over anhydrous Na_2SO_4. Removal of the solvent gave an oil which was purified by preparative TLC using alumina [GF_{254} (type E), E. Merck, A. G.] and hexane–ether (1: 1) to give a colorless viscous liquid of **15** (103 mg); ν_{max} (film) 3450 br., 1680, and 1630 cm^{-1}; λ_{max} 248 nm (ε, 4600); δ 0.90 (3H, d, J=6.9 Hz), 0.95 (3H, d, J=6.9 Hz), 0.94 (3H, s), 1.69 (3H, br. s) and 3.61 (1H, dd, J=6.5 and 9.0 Hz) ppm; *m/e* 236 (M^+) and 193 (Found: *m/e* 236.17911. Calcd for $C_{15}H_{24}O_2$: *m/e* 236.17762).

Acetylation of the α,β-Unsaturated Ketone (**15**). A solution of **15** (84 mg) in pyridine (5 ml) and Ac_2O (1 ml) was allowed to stand at room temperature overnight, and then poured into a cooled 5% HCl aq. solution and extracted with ether. The ethereal extract was washed successively with water, 5% $NaHCO_3$ aq. solution and water, and then dried over anhydrous $MgSO_4$. Removal of the solvent afforded an oil, which was purified by preparative TLC using alumina [GF_{254} (type E), E. Merck, A. G.] and hexane–ether (5: 1) to give a colorless viscous liquid (69 mg), which was completely identical with the acetoxy compound **6** (TLC and IR spectrum).

Mesylation of **15**. To a solution of **15** (93 mg) in pyridine (3 ml) was added dropwise, with stirring, mesyl chloride (50 mg) at 0 °C. The resulting solution was further stirred at 0 °C for 1 h, and then at room temperature for 2 h. After addition of ice–water (*ca.* 10 ml), the solution was extracted with ether. The extract was washed successively with a cooled 5% HCl aq. solution, water and a sat. NaCl aq. solution, and then dried over anhydrous Na_2SO_4. Removal of the solvent under reduced pressure afforded the mesylate **18** (124 mg) in a pure state as a colorless viscous liquid; ν_{max} (film) 1690, 1630, 1350, and 1170 cm^{-1}; λ_{max} 246 nm (ε, 4200); δ 0.89 (3H, d, J=6.5 Hz), 0.95 (3H, d, J=6.5 Hz), 1.00 (3H, s), 1.70 (3H, s), 3.07 (3H, s), and 4.21 (1H, t, J=7.5 Hz) ppm; *m/e* 314 (M^+), 218 and 175 (Found: *m/e* 314.15690. Calcd for $C_{16}H_{26}O_4S$: *m/e* 314.15517).

Reaction of the Mesylate **18** *with NaI*. A mixture of **18** (112 mg) and NaI (530 mg) in methyl ethyl ketone (7 ml) was refluxed, with stirring, for 15 h under a nitrogen atmosphere, and then concentrated under reduced pressure to leave a reddish residue, which was diluted with water (30 ml) and then extracted with ether. The ethereal extract was washed with water, and then dried over anhydrous Na_2SO_4. Removal of the solvent left a reddish oil (120 mg) which was purified by preparative TLC using hexane–benzene (1: 3) to give **19** (36 mg) as a colorless liquid; ν_{max} (film) 1690 and 1630 cm^{-1}; δ 0.88 (3H, d, J=6.3 Hz), 0.93 (3H, d, J=6.3 Hz), 1.11 (3H, s), 1.67 (3H, s), and 4.31 (1H, dd, J=7.0 and 2.0 Hz) ppm; *m/e* 346 (M^+ for $C_{15}H_{23}IO$) and 219 (M^+—I). This iodide was directly used for the next experiment.

Reduction of the Iodide **19** *with* n-Bu_3SnH. To a solution of **19** (36 mg) in toluene (3 ml) was added *n*-Bu_3SnH (26 mg) under a nitrogen atmosphere. The solution was refluxed for 4 h, and then concentrated under reduced pressure to give a yellow oil, which was purified by preparative TLC using hexane–benzene (1: 1) to give a pale yellow liquid (22 mg) which was completely identical with an authentic sample of the isomerization product (**17**) of acolamone[4] (GLC, TLC, and IR spectrum).

Reaction of Epoxyisoacoragermacrone (**2**) *with Basic Alumina*. The compound **2** (980 mg) was dissolved in hexane–benzene (1: 3), and directly chromatographed on basic alumina (Katayama Chemical Co., Ltd., 150—250 mesh) (50 g). Elution with the same solvent system afforded **20** (330 mg) in a pure state as a colorless oil; ν_{max} (film) 3030, 1715, and 1650 cm^{-1}; δ 0.99 (6H, d, J=6.9 Hz), 1.18 (3H, s), 1.86 (3H, br. s), 3.33 (1H, m), 3.77 (1H, br. d, J=7.9 Hz) and 5.88 (1H, br. d, J=7.9 Hz) ppm; *m/e* 436 (M^+), 193, 175, and 165 (Found: *m/e* 236.17941. Calcd for $C_{15}H_{24}O_2$: *m/e* 236.17762).

Further elution with ether afforded a pale yellow oil (450 mg) in an almost pure state, which was further purified by preparative TLC using alumina [GF_{254} (type E), E. Merck, A. G.] and benzene to give **21** in a pure state as a colorless viscous liquid; λ_{max} (film) 3400 br., 3080, 1650, 1600, 915, and 880 cm^{-1}; λ_{max} 240 nm (ε, 16160); δ 0.89 (3H, d, J=6.3 Hz), 0.92 (3H, d, J=6.3 Hz), 1.27 (3H, s), 3.38 (1H, br. m), 4.32 (1H, dd, J=6.5 and 9.5 Hz), 4.67 (1H, br. m), 4.79 (1H, d, J=2.4 Hz), and 5.58 (1H, s) ppm; *m/e* 236 (M^+ for $C_{15}H_{24}O_2$), 221 and 193. Elemental analysis of **21** was not carried out because of its instability, but its structure may be supported by the above-mentioned physical data.

Catalytic Hydrogenation of **20**. Catalytic hydrogenation of **20** (45 mg) in MeOH (10 ml) was carried out over 5% Pd–C (150 mg) at room temperature for 40 min, and then filtered to remove the catalyst. The filtrate was concentrated under reduced pressure to give a colorless viscous liquid which was chromatographed on alumina and eluted with ether to give the dihydro compound **22** (38 mg) as colorless crystals; mp 37—40 °C (by sublimation); ν_{max} (KBr) 1705 cm^{-1}; δ 0.94 (6H, d, J=7.1 Hz), 1.08 (3H, d, J=6.5 Hz), 1.23 (3H, s), and 3.27 (1H, m) ppm; *m/e* 238 (M^+), 210, 195, 182, and 167 (found: *m/e* 238.19233. Calcd for $C_{15}H_{26}O_2$: *m/e* 238.19327).

Epoxidation of Isoacoragermacrone (**1**) *with 30% H_2O_2–5% aq. NaOH*. To a solution of **1** (440 mg) in MeOH (30 ml) was slowly added a mixed solution of 30% H_2O_2 (2 ml) and 5% NaOH aq. solution (10 ml) at 0 °C, and then the reaction temperature was gradually elevated to room temperature. The solution was further stirred at room temperature overnight, and then diluted with water (60 ml) and extracted with ether. The ethereal extract was washed with water, and then dried over anhydrous $MgSO_4$. Removal of the solvent afforded a colorless viscous liquid (436 mg), which was crystallized from hexane to give colorless prisms of **23**; mp 85.5—86 °C; ν_{max} (KBr) 1720 cm^{-1}; δ 0.90 (3H, d, J=7 Hz), 1.04 (3H, d, J=7 Hz), 1.42 (3H, s), 1.44 (3H, s), 3.43 (1H, s) and 5.20 (1H, t, J=7 Hz) ppm (Found: *m/e* 236.17474. Calcd for $C_{15}H_{24}O_2$: *m/e* 236.17762).

Reaction of **23** *with 80% aq. AcOH*. A solution of **23** (23 mg) in 80% aq. AcOH (0.5 ml) was heated at 60 °C for 3 h,

with stirring. After addition of ether (20 ml), the solution was washed successively with a sat. $NaHCO_3$ aq. solution and a sat. NaCl aq. solution, and then dried over anhydrous $MgSO_4$. Removal of the solvent afforded a colorless liquid (25 mg), which was recrystallized from ether to give colorless crystals (10 mg). The remaining ethereal solution was concentrated, and then separated by preparative TLC to give colorless crystals (2 mg). Recrystallization from $CHCl_3$ afforded colorless prisms of **24**; mp 195 °C (decomp.); ν_{max} (KBr) 3400 cm^{-1}; δ 0.92 (3H, d, J=7 Hz), 0.94 (3H, d, J=7 Hz), 1.32 (3H, s), 1.56 (1H, s, OH), 1.73 (3H, br. s), 2.16 (2H, s, OH), 3.90 (1H, br. s) and 5.64 (1H, m) ppm; *m/e* 254 (M^+) and 236 (Found: C, 70.27; H, 10.50%. Calcd for $C_{15}H_{26}O_3$: C, 70.83; H, 10.30%).

Reaction of 23 with 80% aq. HCOOH. A solution of **23** (120 mg) in 80% aq. HCOOH (2 ml) was stirred at room temperature for 10 min, and then diluted with ether (40 ml). The ethereal solution was washed successively with water, a sat. $NaHCO_3$ aq. solution and a sat. NaCl aq. solution, and then dried over anhydrous $MgSO_4$. Removal of the solvent afforded a colorless viscous liquid which was dissolved in ether (0.5 ml) to give the triol **24** (10 mg) as colorless crystals. After filtration of the crystals, the filtrate was subjected to preparative TLC using $CHCl_3$ to give the formate **25** (22 mg) as a colorless viscous liquid; ν_{max} (film) 3470 and 1720 cm^{-1}; δ 0.93 (3H, d, J=7 Hz), 0.96 (3H, d, J=7 Hz), 1.66 (3H, s), 1.74 (3H, br.s), 2.49 (1H, s, OH), 3.96 (1H, d, J=5.4 Hz), 5.65 (1H, m), and 8.04 (1H, s) ppm; *m/e* 236 (M^+—HCOOH), 218, and 200. Without purification this formate was used for the next experiment.

Hydrolysis of the Formate (25) with 10% Methanolic KOH. A solution of **25** (22 mg) in 10% methanolic KOH (5 ml) was stirred at room temperature overnight, and then diluted with ether (30 ml). The ethereal solution was washed with water, and then dried over anhydrous Na_2SO_4. Removal of the solvent gave colorless crystals of **24** (mp and IR spectrum).

Oxidation of the Triol (24) with $NaIO_4$. To a solution of **24** (90 mg) in MeOH (6 ml) was added, with stirring, a solution of $NaIO_4$ (230 mg) in water (3 ml). The resulting solution was further stirred at room temperature overnight, and then diluted with water (20 ml) and extracted with ether. The ethereal extract was washed successively with water and a sat. NaCl aq. solution, and then dried over anhydrous $MgSO_4$. After evaporation of the solvent, the oily residue was separated by preparative TLC using $CHCl_3$ to give the oxidation product **26** (18 mg) in addition to the starting material (20 mg) (TLC and IR spectrum).

26. A colorless viscous liquid: ν_{max} (film) 1720 br.cm^{-1}; δ 0.86 (3H, d, J=6.5 Hz), 0.93 (3H, d, J=6.5 Hz), 1.26 (3H, s), 2.12 (3H, s), 3.03 (1H, dd, J=10 and 2 Hz) and 8.00 (1H, s) ppm; *m/e* 222 [M^+($C_{15}H_{24}O_4$)—HCOOH]. This compound was further used for the next experiment.

Formation of an α,β-Unsaturated Ketone 27. A solution of **26** (18 mg) in MeOH (4 ml) containing NaOMe (10 mg) was refluxed for 4 h under a nitrogen atmosphere, and then diluted with water (10 ml) and extracted with ether. The ethereal solution was washed with water, and then dried over anhydrous $MgSO_4$. Evaporation of the solvent gave a colorless oil, which was purified by preparative TLC using $CHCl_3$ to afford **27** (14 mg) in a pure state as a colorless liquid; δ (C_6D_6) 0.86 (3H, d, J=7.0 Hz), 0.91 (3H, d, J=7.0 Hz), 1.56 (3H, s), 1.72 (3H, s), 2.30 (2H, t, J=7.8 Hz), and 2.65 (2H, t, J=7.8 Hz) ppm (Found: *m/e* 222.16433. Calcd for $C_{14}H_{22}O_2$: *m/e* 222.16197).

Reaction of 23 with $AlCl_3$. To a solution of **23** (190 mg) in absolute ether (10 ml) was added, with stirring, a solution of $AlCl_3$ (118 mg) in absolute ether (2 ml) at 0 °C. The solution was further stirred at 0 °C for 10 min, and then the reaction was quenched by addition of ice-water (0.5 ml). After addition of a sat. potassium sodium tartarate aq. solution (10 ml), the ethereal layer was separated. The aqueous solution was further extracted with ether. The combined ethereal extracts were washed with water, and then dried over anhydrous $MgSO_4$. Evaporation of the solvent afforded a colorless viscous liquid, which was separated by preparative TLC using benzene to give **28** (52 mg) and **29** (60 mg).

28. A colorless viscous liquid: ν_{max} (film) 2700 and 1720 cm^{-1}; δ 0.91 (3H, d, J=7 Hz), 0.98 (3H, d, J=7 Hz), 1.25 (3H, s), 1.52 (3H, s), and 9.75 (1H, s) ppm (Found: *m/e* 236.17748. Calcd for $C_{15}H_{24}O_2$: *m/e* 236.17762).

29. A colorless viscous liquid: ν_{max} (film) 3560, 3090, and 1650 cm^{-1}; δ 0.87 (3H, d, J=7 Hz), 0.90 (3H, d, J=7 Hz), 1.67 (3H, s), 2.90 (1H, d, J=12 Hz), 3.31 (1H, d, J=12 Hz), 4.66 (1H, br. s), and 4.86 (1H, br. s) ppm (Found: *m/e* 236.17253. Calcd for $C_{15}H_{24}O_2$: *m/e* 236.17762).

Reduction of the Aldehyde (28) with $LiAlH_4$. To a solution of **28** (55 mg) in absolute THF (5 ml) was added, with stirring, $LiAlH_4$ (20 mg) at room temperature. The reaction mixture was further stirred at room temperature overnight. After decomposition of an excess of the reagent with water, the reaction mixture was diluted with 5% HCl aq. solution, and then extracted with ether. The ethereal extract was washed with water, and then dried over anhydrous $MgSO_4$. After evaporation of the solvent, a colorless oil was purified by preparative TLC using $CHCl_3$ to give **30** (35 mg) as a colorless viscous liquid; ν_{max} (film) 3400 cm^{-1}; δ 0.98 (3H, d, J=6 Hz), 1.03 (3H, d, J=6 Hz), 1.24 (6H, s), 3.56 (1H, d, J=12 Hz), and 3.76 (1H, d, J=12 Hz) ppm (Found: *m/e* 238.19307. Calcd for $C_{15}H_{26}O_2$: *m/e* 238.19327).

Acetylation of the Alcohol (30). A solution of **30** (35 mg) in pyridine (3 ml) and Ac_2O (1 ml) was stirred at room temperature overnight, and then treated as usual to give a pale yellow oil, which was purified by preparative TLC using $CHCl_3$ to give **31** (25 mg) as a colorless viscous liquid; ν_{max} (film) 1740 and 1240 cm^{-1}; δ 0.94 (3H, d, J=7 Hz), 0.97 (3H, d, J=7 Hz), 1.24 (3H, s), 1.28 (3H, s), 2.07 (3H, s), and 4.10 (2H, br. s) ppm (Found: *m/e* 280.20383. Calcd for $C_{17}H_{28}O_3$: *m/e* 280.20433).

Hydrolysis of the Acetate (31). A solution of **31** (25 mg) in 5% methanolic KOH (2 ml) was stirred at room temperature overnight, and then diluted with water (10 ml) and extracted with ether. The ethereal extract was washed with water and then dried over anhydrous $MgSO_4$. Removal of the solvent afforded the original alcohol (**30**) (TLC and IR spectrum) as a colorless liquid.

Oxidation of 30. Jones' reagent was carefully added to a solution of **30** (25 mg) in acetone (4 ml) until a brown color appeared persistently. The mixture was stirred at room temperature for 1.5 h, and then diluted with water (10 ml) after decomposition of an excess of the reagent with 30% ascorbic acid aq. solution. The aqueous solution was extracted with ether. The ethereal extract was washed with water, and then dried over anhydrous $MgSO_4$. Removal of the solvent gave an almost colorless oil, which was purified by preparative TLC using benzene to afford **28** (13 mg) (TLC and IR spectrum) as a colorless viscous liquid.

Catalytic Hydrogenation of 29. Catalytic hydrogenation of **29** (28 mg) in AcOEt (3 ml) was carried out over PtO_2 at room temperature for 1.5 h, and then filtered to remove the catalyst. The filtrate was concentrated under reduced pressure to give a colorless viscous liquid, which was purified by preparative TLC using hexane–benzene (1: 1) to give the

dihydro compound (**32**) as a colorless viscous liquid; ν_{max} (film) 3560 cm^{-1}; δ 0.90 (3H, d, J=7 Hz), 0.92 (3H, d, J=7 Hz), 1.10 (3H, d, J=8 Hz), 1.64 (3H, s), 2.85 (1H, m), 2.86 (1H, d, J=12 Hz), and 3.18 (1H, d, J=12 Hz) ppm (Found: *m/e* 238.19088. Calcd for $C_{15}H_{26}O_2$: *m/e* 238.19327).

Reaction of ***33*** *with 80% aq. AcOH.* A solution of **33** (60 mg) in 80% aq. AcOH (1 ml) was heated, with stirring, at 80 °C for 4 h, and then diluted with water (15 ml) and extracted with $CHCl_3$. The extract was washed successively with water, a sat. $NaHCO_3$ aq. solution and water, and then dried over anhydrous $MgSO_4$. Removal of the solvent afforded a pale brown oil, which was separated by preparative TLC using benzene–ether (3: 1) to give **34** (9 mg) as a colorless viscous liquid; *m/e* 276 (M^+-H_2O), 234 (M^+—AcOH), and 216 (Found: *m/e* 234.16179. Calcd for $C_{15}H_{22}O_2$ ($C_{17}H_{26}O_4$–AcOH): *m/e* 234.16197).

Reaction of ***33*** *with $AlCl_3$ in Absolute Ether.* To a solution of **33** (120 mg) in absolute ether (20 ml) was added, with stirring, a solution of $AlCl_3$ (60 mg) in absolute ether (10 ml) at −5 °C. The solution was further stirred at −5 °C, and then the reaction was quenched by addition of ice–water (*ca.* 1 ml). The ethereal layer was separated, and dried over anhydrous $MgSO_4$. After evaporation of the solvent, an oily residue was separated by preparative TLC using benzene–ether (3: 1) to give **34** (48 mg) (TLC and IR spectrum) as a colorless viscous liquid.

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