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Chemical Transformation of Terpenoids. V.[1] Acidic Conversions of 10-Hydroxygeraniol and 10-Hydroxynerol Derivatives Leading to Cyclic Monoterpenoids

ISAO KITAGAWA,* SHINJI TSUJII, FUMIKO NISHIKAWA (*née* MIYAMOTO), and HIROTAKA SHIBUYA

Faculty of Pharmaceutical Sciences, Osaka University, 1–6, Yamada-oka, Suita, Osaka 565, Japan

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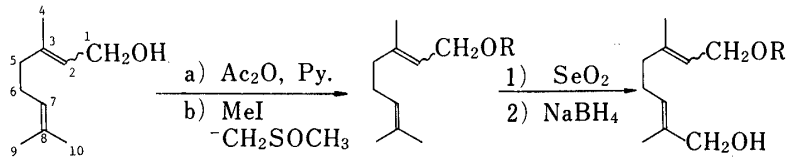
Acid treatment of 1-*O*-acetyl-10-hydroxygeraniol (**5a**), 1-*O*-methyl-10-hydroxygeraniol (**5b**), 1-*O*-acetyl-10-hydroxynerol (**6a**), and 1-*O*-methyl-10-hydroxynerol (**6b**) was investigated under various conditions. It was found that treatment of **5a** and **6a** with HCOOH gave menth-1-ene-8,9-diol (**7**), while treatment of **5a**, **5b**, **6a**, or **6b** with BF_3-etherate in CH_2Cl_2 furnished two menthofuran-type compounds (**9**, **10**) and two bicyclo[3.2.1]oct-2-ene derivatives (**17**, **24**). Both **9** and **10** were successfully converted to menthofuran (**16**) and **17** was converted to a bicyclo[3.2.1]octenone derivative (**23**) which was a key intermediate for a synthesis of juvabione (**27**).

Keywords——geraniol; nerol; 10-hydroxygeraniol; 10-hydroxynerol; 10-hydroxygeraniol derivative; 10-hydroxynerol derivative; uroterpenol; menthofuran; bicyclo[3.2.1]oct-2-ene derivative

Chemical cyclization reactions of acyclic terpenoids are of interest from the view point of biomimetic reactions, since some acyclic terpenoids have been shown to be biogenetic precursors for various naturally occurring cyclic terpenoids. Hitherto reported cyclization studies, in which terpenoid alcohols were used as starting materials, may be classified into the following categories: 1) cyclization reactions mimicking biogenetic pathways,[2] 2) cyclizations by means of "ene" reactions,[3] and 3) cyclizations by the use of organometallic reagents[4] or superacid.[5] As part of a continuing series of studies on the biogenetically patterned transformation of terpenoids,[6] we have investigated the chemical behavior of four derivatives of 10-hydroxygeraniol (**5**) and 10-hydroxynerol (**6**) which are key compounds in the biosynthetic pathways to various cyclopentanoid monoterpenes (*e.g.* iridoids).[7] This paper deals with the structure elucidation of various cyclization products formed during the acidic treatment of 1-*O*-acetyl-10-hydroxygeraniol (**5a**), 1-*O*-methyl-10-hydroxygeraniol (**5b**), 1-*O*-acetyl-10-hydroxynerol (**6a**), and 1-*O*-methyl-10-hydroxynerol (**6b**).

Starting Materials

The oxidation of geranyl acetate (**3a**) and geranyl methyl ether (**3b**), which were prepared from geraniol (**1**) by ordinary acetylation and methylation, with selenium oxide in ethanol followed by sodium borohydride reduction furnished 1-*O*-acetyl-10-hydroxygeraniol (**5a**, 69% from **1**) and 1-*O*-methyl-10-hydroxygeraniol (**5b**, 46% from **1**). Similarly, 1-*O*-acetyl-10-hydroxynerol (**6a**, 60% from **2**) and 1-*O*-methyl-10-hydroxynerol (**6b**, 47% from **2**) were synthesized from nerol (**2**) *via* neryl acetate (**4a**) and neryl methyl ether (**4b**), respectively. The structures of these four 10-hydroxy derivatives (**5a**, **5b**, **6a**, and **6b**) were substantiated by their physicochemical properties (see "Experimental") and by mechanistic consideration of the selenium oxide oxidation.[8]



1 [2*E*]: geraniol
2 [2*Z*]: nerol

3a [2*E*]: R=Ac
3b [2*E*]: R=CH_3
4a [2*Z*]: R=Ac
4b [2*Z*]: R=CH_3

5 [2*E*]: R=H
5a [2*E*]: R=Ac
5b [2*E*]: R=CH_3

6 [2*Z*]: R=H
6a [2*Z*]: R=Ac
6b [2*Z*]: R=CH_3

Chart 1

Formic Acid Treatment

After preliminary examinations of acid treatment of 1-*O*-acetyl-10-hydroxygeraniol (**5a**) under various reaction conditions, it was found that formic acid treatment of **5a** (at room temperature for 2 h) followed by alkaline hydrolysis gave in 92% yield an oily product (**7**) which was found to be a *ca.* 3:2 mixture of two racemic diastereomers.[9]

The infrared (IR) spectrum of **7** showed hydroxyl and olefinic absorption bands, while the proton nuclear magnetic resonance (^{1}H NMR) spectrum showed signals ascribable to one tertiary methyl group, one vinylic methyl group, one primary carbinyl methylene function attached to a quaternary carbon, and one olefinic proton. Thus, the plane structure, menth-1-ene-8,9-diol (**7**), which was formerly proposed for uroterpenol,[10] was assigned to the product. The assignment was substantiated by the conversion of **7** to (±)-α-terpineol (**8**) *via* tosylation followed by lithium aluminum hydride reduction.

The ratio (*ca.* 3:2) of the two isomers in the product **7** was deduced from their 8-CH_3 signals, which were observed at δ 1.00 (s, 3H × 3/5) and δ 1.03 (s, 3H × 2/5). The formation of this isomeric mixture can be rationalized on the basis of an intermediate carbonium ion (iii) which may be formed *via* i⇄ii. When this racemic cation iii is depicted as epimeric perspective structures, *i.e.*, A with 4(*R*) and B with 4(*S*), nonequivalent attacks of hydroxyl anion from both sides of the C-8 cation (iii) can be rationalized. Hydroxyl anion attacks shown by a solid arrow in A and B would give one racemic pair of diastereomers **7** [4(*R*), 8(*R*) and 4(*S*), 8(*S*)], while the other attacks shown by an empty arrow would give another racemic pair of diastereomers **7** [4(*R*), 8(*S*) and 4(*S*), 8(*R*)].

Similar formic acid treatment of 1-*O*-acetyl-10-hydroxynerol (**6a**) followed by alkaline hydrolysis provided the same diastereomeric mixture of **7** in 79% yield. However, in the cases of 1-*O*-methyl-10-hydroxygeraniol (**5b**) and 1-*O*-methyl-10-hydroxynerol (**6b**), acid treatment resulted in the formation of complex mixtures.

BF_3-Etherate Treatment

Treatment of **5a**, **5b**, **6a**, or **6b** with BF_3-etherate in methylene chloride provided a mixture of four products: P-1 (**9**), P-2 (**10**), P-3 (**17**), and P-4 (**24**).[11] As shown in Table I, the percentage compositions of these products varied depending upon the starting compounds. The 2*E* geraniol derivatives (**5a**, **5b**) provided P-3 (**17**) as the major product, while the 2*Z* nerol derivatives (**6a**, **6b**) gave P-1 (**9**) as the major product.

P-1 (**9**) was a colorless oily compound. The IR spectrum showed the double bond absorption band, while the ^{1}H NMR spectrum showed signals ascribable to one secondary methyl group, one vinylic methyl group, an olefinic proton, methylene protons and a methine proton attached to carbon bearing an oxygen function. Furthermore, spin-decoupling experiments indicated adjacency of the olefinic proton and the methine proton: irradiation at δ 5.36 (7-H) changed a triplet-like signal at δ 4.10 (7a-H) to a doublet ($J_{3a,7a}$ = 5 Hz). Thus, a

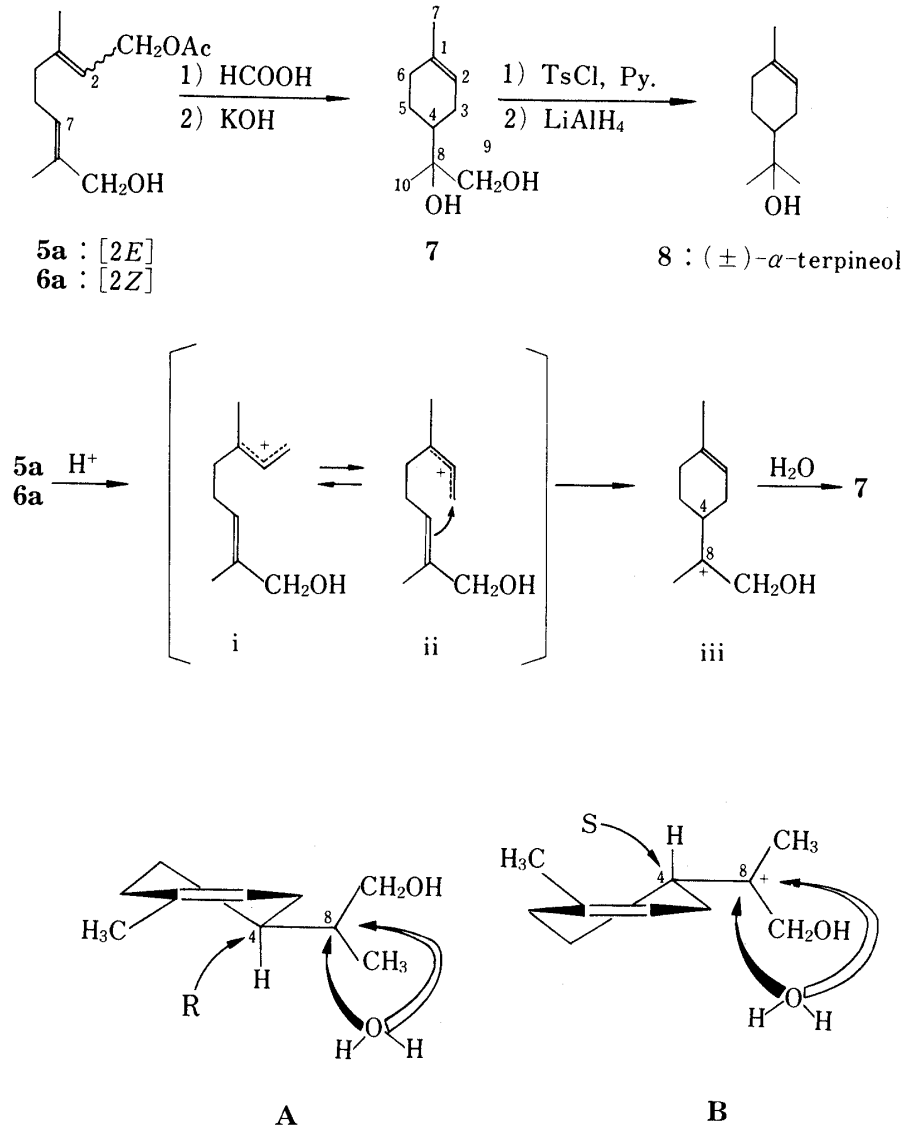


Chart 2

TABLE I. Percentage Compositions of Products Obtained by BF_3-Etherate Treatment of **5a**, **5b**, **6a**, and **6b**[a]

Starting materials	Products				
	P-1 (**9**)	P-2 (**10**)	P-3 (**17**)	P-4 (**24**)	Others[b]
5a	14	8	43	7	28
5b	25	17	50	8	—
6a	37	19	17	3	21
6b	47	23	21	9	—

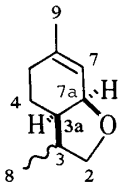
a) Determined by gas liquid chromatography (GLC): column HB-2000, 0.25 mm × 45 m; column temp., 130 °C; N_2 flow rate, 0.5 ml/min.
b) The structures of these products have not yet been clarified.

cis-fused menthofuran-type structure C, in which the C-3 configuration is undetermined, can be assigned to P-1.

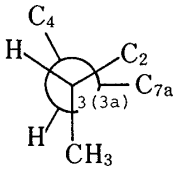
P-2 (**10**) was also a colorless oily compound and an isomer of P-1. The IR and ^1H NMR spectra showed the presence of functions similar to those in P-1. Here again, the ^1H NMR

decoupling experiments indicated adjacency of the olefinic proton and the methine proton on a carbon bearing an oxygen function: irradiation at δ 5.46 (7-H) changed a triplet-like signal at δ 4.01 (7a-H) to a doublet ($J_{3a,7a}=4$ Hz). Therefore, the structure C is also assignable to P-2, and P-1 and P-2 are presumed to be epimeric at C-3.

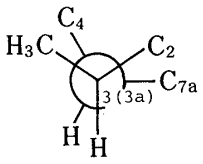
In regard to the C-3 configurations in P-1 and P-2, the carbon-13 nuclear magnetic resonance (^{13}C NMR) spectra of both compounds defined the 3α-methyl structure **9** for P-1 and the 3β-methyl structure **10** for P-2 on the basis of the following findings. The signals due to 4-C and 8-C in P-1 were observed at δ 23.83 (t) and δ 17.54 (q), while those in P-2 were seen at δ 19.10 (t) and δ 11.70 (q), which indicated the presence of greater steric compression[12] between 4-C and 8-C in P-2 (**10**) than between those carbons in P-1 (**9**), as shown in their Newman projections.



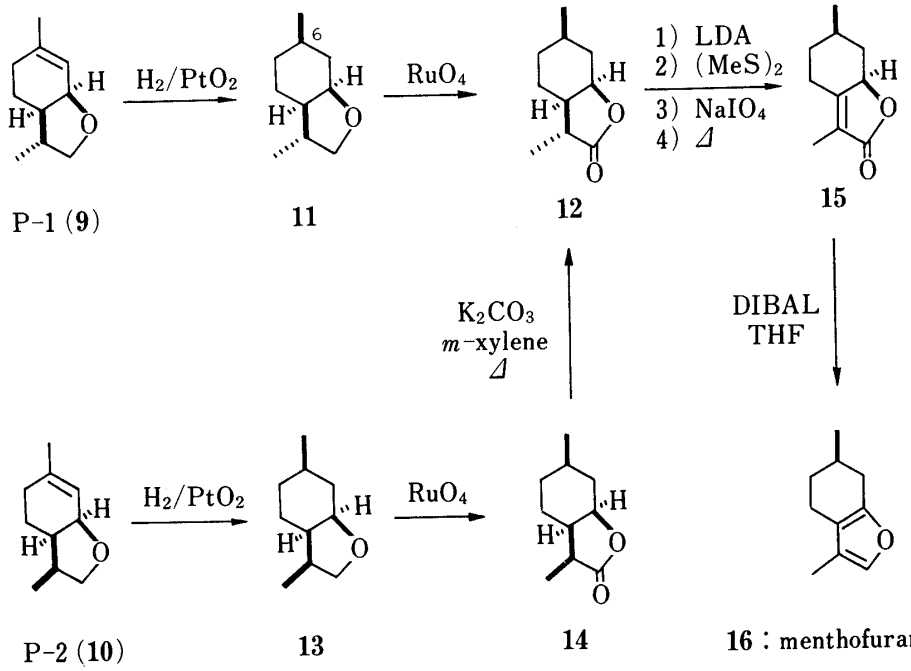
C



P-1 (**9**)



P-2 (**10**)



P-1 (**9**) **11** **12** **15**

P-2 (**10**) **13** **14** **16** : menthofuran

Chart 3

In order to prove chemically the epimeric relationship of P-1 (**9**) and P-2 (**10**) and to establish their structures, the following chemical conversions were carried out. Catalytic hydrogenation of P-1 (**9**) over platinum dioxide quantitatively gave a dihydro derivative **11**, in which the 6β-methyl configuration was assigned on the basis of stereochemical consideration of the hydrogenation. Ruthenium tetroxide oxidation of **11** provided a γ-lactone derivative **12** in 96% yield. On the other hand, similar catalytic hydrogenation of P-2 (**10**) afforded a dihydro compound **13** in 79% yield. Successive ruthenium tetroxide oxidation of **13** provided another γ-lactone **14** in 48% yield. Two γ-lactone derivatives thus prepared were isomeric. The IR spectra taken in carbon tetrachloride showed absorption bands at 1785 cm^{-1} for **12** and

1777 cm^{-1} for **14**. The ^1H NMR spectra of both γ-lactones indicated loss of signals due to methylene protons in the tetrahydrofuran rings. Heating of both γ-lactones with dry potassium carbonate in *m*-xylene disclosed different stabilities. The γ-lactone **12** was unchanged under these reaction conditions, while the γ-lactone **14** was quantitatively isomerized to **12**. Thus, the less stable 3β-methyl configuration was chemically elucidated for P-2 (**10**).

Finally, P-1 (**9**) was converted to (±)-menthofuran (**16**)[13] in the following short sequence. The γ-lactone **12**, which was prepared above from **9**, was converted to the butenolide (**15**) according to a procedure reported by Trost and Salzmann[14] in 80% yield. The structure **15** was supported by the physicochemical properties: the IR and the ultraviolet (UV) spectra and the ^1H NMR spectrum, which showed signals assignable to the vinylic 3-methyl group (δ 1.72, t, $J=1$ Hz) and 7a-H (δ 4.52, dd, $J=6$, 10 Hz). Reduction of the butenolide (**15**) with diisobutyl aluminum hydride (DIBAL) in tetrahydrofuran[15] provided a furano compound (**16**) in 77% yield, and the product was found to be identical with authentic (+)-menthofuran except for the optical activity.

The third product P-3 (**17**) was a colorless oily compound. The IR spectrum showed hydroxyl and double bond absorption bands. The ^1H NMR spectrum showed the presence of one secondary methyl group, one vinylic methyl group, one carbinyl methine proton (dd, $J=4$, 6 Hz), and an olefinic proton. ^1H NMR shift experiments with P-3 using $Eu(dpm)_3$ disclosed that the carbinyl methine proton (7-H), a proton (6-H) geminal to the secondary methyl group, and an allylic methine proton (1-H) are in close proximity since signals due to these protons were shifted significantly to low field on addition of the shift reagent (Table II).

Acetylation of P-3 (**17**) yielded the monoacetate (**18**), which, on ozone oxidation, was converted to a keto-aldehyde (**19**). Since an aldehydic proton in **19** was observed as a triplet ($J=2$ Hz) at δ 9.88 in the ^1H NMR spectrum, the presence of a methylene moiety adjacent to the aldehyde function is indicated. Methylation of P-3 (**17**) with methyl iodide and sodium hydride provided the monomethyl ether (**20**). Hydroboration–oxidation of **20** followed by pyridinium chlorochromate (PCC) oxidation[16] furnished a six-membered ring ketone (**21**). On the other hand, another ketone (**22**), which was obtained by PCC oxidation of P-3 (**17**), was shown to be a five-membered ring ketone by its IR spectrum.

Based on the above-mentioned evidence, the structure of P-3 (**17**) was formulated as 2,6-dimethyl-7-hydroxy-bicyclo[3.2.1]oct-2-ene. The *endo* 7-hydroxy configuration in P-3 was assigned on the basis that sodium borohydride reduction of the ketone (**22**) in methanol–ether (1 : 10) resulted in recovery of P-3 (**17**), since hydride attack on **22** was considered to occur from the convex side. Furthermore, the *exo* 6-methyl configuration in P-3 is supported by the fact that treatment of the ketone (**22**) with lithium diisopropylamide (LDA) followed by protonation with acetic acid under kinetic conditions[17] furnished the 6-epimer (**23**) predominantly (**22** : **23** = 1 : 14).

TABLE II. ^1H NMR Data for P-3 (**17**) Taken in CCl_4 without and with $Eu(dpm)_3$

	In CCl_4	In CCl_4 with 0.15 eq $Eu(dpm)_3$	$\Delta\delta$ (ppm)
1-H	2.21	4.82	2.61
3-H	5.22	6.62	1.40
6-H	*ca.* 1.5	5.44	*ca.* 3.9
7-H	3.69	8.87	5.18
2-CH_3	1.72	3.33	1.61
6-CH_3	1.07	2.34	1.27

P-4 (**24**) was also a colorless oily compound and was an isomer of P-3 (**17**). The presence of functions in P-4 similar to those in P-3 (**17**) was apparent from the IR and ^{1}H NMR spectra, and thus P-4 was presumed to possess a structure similar to that of P-3. This was verified by quantitative conversion of the ketone (**23**), which was prepared from P-3 as described above, to P-4 by sodium borohydride reduction in methanol–ether (1 : 10). Thus, P-4 (**24**) has been proved to be the 6-methyl epimer of P-3 (**17**).

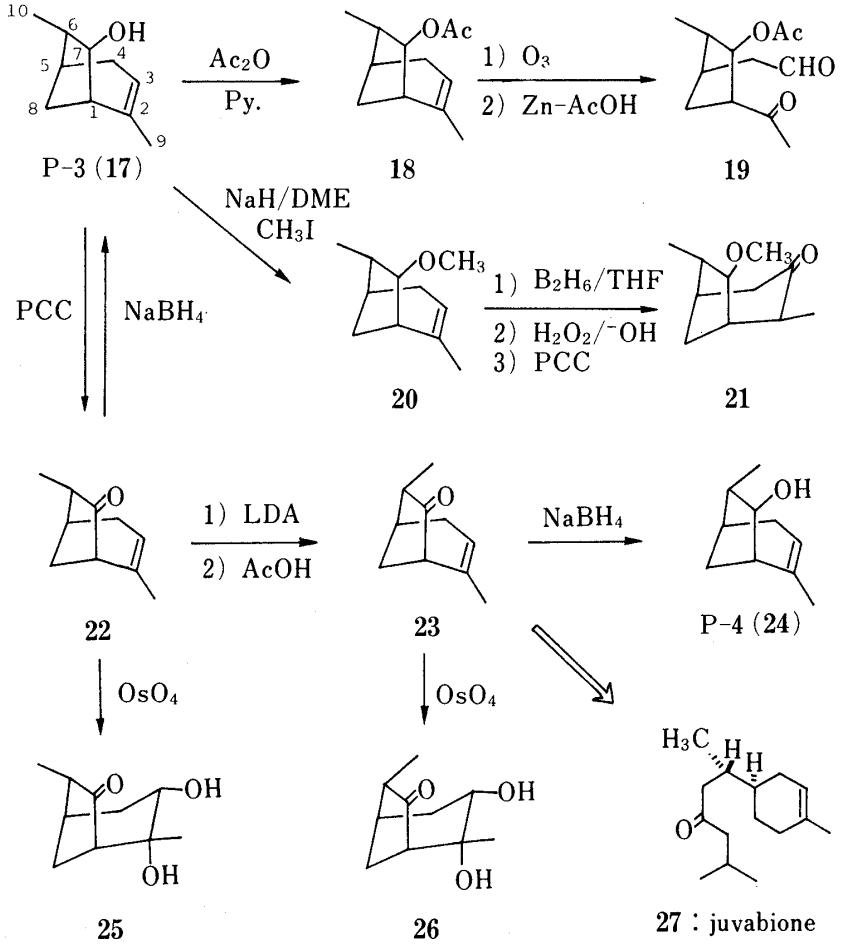


Chart 4

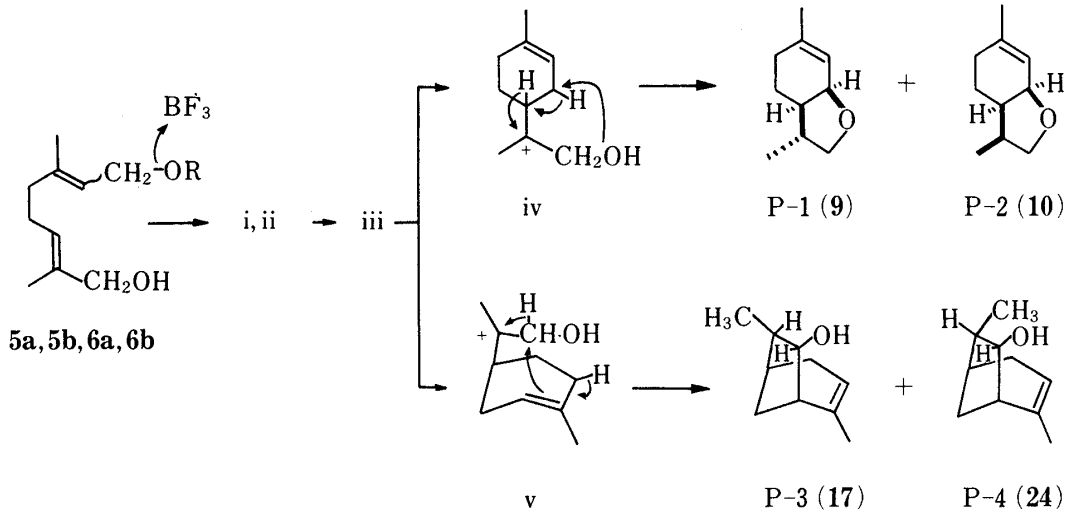


Chart 5

In order to obtain more definite evidence for the structures of P-3 (**17**) and P-4 (**24**), the following conversions were carried out. Oxidation of two isomeric ketones (**22**, **23**) with osmium tetroxide in pyridine provided the corresponding keto-diols, **25** and **26**. Of these two crystalline products, the physicochemical properties of **25** were found to be identical with those of the compound previously reported by Larsen and Monti.[18] Furthermore, the ketone (**23**), which was prepared from P-3 (**17**) in the present study, was found to be identical with a compound prepared as a key intermediate for a synthesis of (±)-juvabione (**27**).[17,19] The reaction pathways to P-1 (**9**), P-2 (**10**), P-3 (**17**), and P-4 (**24**) from **5a**, **5b**, **6a**, and **6b** may be expressed as shown in Chart 5.

In conclusion, acid treatments of acyclic monoterpene derivatives, *i.e.*, 1-*O*-acetyl-10-hydroxygeraniol (**5a**), 1-*O*-methyl-10-hydroxygeraniol (**5b**), 1-*O*-acetyl-10-hydroxynerol (**6a**), and 1-*O*-methyl-10-hydroxynerol (**6b**), resulted in the formation of cyclic monoterpene derivatives, *i.e.*, menth-1-ene-8,9-diol (**7**) on formic acid treatment and two menthofuran-type compounds (**9**, **10**) and two bicyclo[3.2.1]oct-2-ene derivatives (**17**, **24**) on BF_3-etherate treatment. The reason for these differences in the products depending upon the reaction conditions is unclear. It is noteworthy that **9** and **10** were conveniently converted to (±)-menthofuran, while **17** was converted to **23**, a key synthetic intermediate for (±)-juvabione (**27**). Thus, formal syntheses of (±)-menthofuran and (±)-juvabione from geraniol (**1**) and nerol (**2**) have been accomplished.

Experimental

The following instruments were used to obtain physical data: melting points, Yanagimoto micro-melting point apparatus (values are uncorrected); IR spectra, Hitachi EPI-G3 infrared spectrometer; UV spectra, Hitachi EPS-3T spectrophotometer; mass spectra (MS), Hitachi RMU-6D mass spectrometer; high resolution MS, JEOL JMS-01SG mass spectrometer; ^{1}H NMR spectra, Hitachi R-22 NMR spectrometer (90 MHz, in CCl_4); ^{13}C NMR spectra, JEOL FX-100 FT-NMR spectrometer. Chromatography was carried out as follows: gas-liquid chromatography (GLC), with a Hitachi gas chromatograph model 163 or model 164; thin-layer chromatography (TLC), on pre-coated TLC plates (Merck Kieselgel 60F-254), detection by spraying with 1% $Ce(SO_4)_2$–10% aq. H_2SO_4 followed by heating; column chromatography, with silica gel (Merck Kieselgel 60, 70—230 mesh).

1-*O*-Acetyl-10-hydroxygeraniol (5a) from Geraniol (1)——An ice-cooled solution of geraniol (**1**, 48 g) in Ac_2O (50 ml) and pyridine (50 ml) was left standing for 1.5 h. The reaction mixture was poured into ice-water and the whole was extracted with EtOAc. After usual work-up of the EtOAc extract, the solvent was evaporated off under reduced pressure to yield an oily product. Column chromatography (SiO_2 1.5 kg, hexane : EtOAc = 20 : 1) of the product afforded geranyl acetate (**3a**, 58.5 g). A solution of **3a** (58.5 g, 0.30 mol) in 99% EtOH (100 ml) was treated with a solution of SeO_2 (35.0 g, 0.31 mol) in 80% EtOH (300 ml) and the whole was heated under reflux for 1 h. Concentration of the yellow-green reaction mixture under reduced pressure to a volume of *ca.* 90 ml gave a suspension, which was treated with ether (100 ml). After removal of the insoluble material by filtration, the ethereal solution was washed successively with aq. sat. $NaHCO_3$ and aq. sat. NaCl, then dried over $MgSO_4$. After being concentrated to *ca.* 100 ml, the solution was treated with MeOH (10 ml). The mixture was ice-cooled and then treated dropwise with a suspension of $NaBH_4$ (6.1 g, 0.16 mol) in ether–MeOH (10 : 1, 150 ml) during a period of 30 min. After being stirred for a further 15 min under ice-cooling, the reaction mixture was treated with aq. 5% HCl and the whole was extracted with EtOAc. The EtOAc extract was washed successively with aq. sat. $NaHCO_3$ and aq. sat. NaCl, then dried over $MgSO_4$. Removal of the solvent under reduced pressure gave a yellow oily product (50.0 g). Column chromatography (SiO_2 2.5 kg, hexane : EtOAc = 5 : 1) of the product furnished 1-*O*-acetyl-10-hydroxygeraniol (**5a**, 45.7 g, 69% from **1**). **5a**, colorless oil, bp 129 °C (3 mmHg). *Anal.* Calcd for $C_{12}H_{20}O_3$: C, 67.89; H, 9.50. Found: C, 67.97; H, 9.53. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3600, 3500 (br), 1740, 1665. ^{1}H NMR (δ): 1.61 (3H, br s, 9-H_3), 1.70 (3H, br s, 4-H_3), 1.98 (3H, s, $OCOCH_3$), 2.90 (1H, br s, OH, exchangeable with D_2O), 3.86 (2H, br s, 10-H_2), 4.49 (2H, d, J = 7 Hz, 1-H_2), 5.27 (2H, m, 2-H, 7-H). MS *m/z* (%): 152 ($M^+ - AcOH$, 5), 43 (100).

Geranyl Methyl Ether (3b) from Geraniol (1)——A solution of **1** (7.2 g) in DMSO (110 ml) was treated with a dimsyl carbanion DMSO solution (prepared from 52.9% NaH 5.0 g and DMSO 50 ml) and the whole solution was stirred at room temp. (26 °C) for 1 h. Under ice-cooling, the solution was treated with CH_3I (15 ml) and the whole was stirred again at room temp. for 1 h. The reaction mixture was poured into ice-water and the whole was extracted with EtOAc. The EtOAc extract was then washed successively with aq. 5% HCl, aq. sat. $NaHCO_3$, and aq. sat. NaCl, then dried over $MgSO_4$. Removal of the solvent under reduced pressure yielded a yellow oily product (8.3 g) which was

purified by distillation under reduced pressure to furnish geranyl methyl ether (**3b**, 5.5 g, 80%). **3b**, colorless oil, bp 61 °C (3 mmHg). *Anal.* Calcd for $C_{11}H_{20}O$: C, 78.51; H, 11.98. Found: C, 78.48; H, 11.91. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1665. ^1H NMR (δ): 1.59 (3H, br s, 9-H_3), 1.63 (3H, br s, 4-H_3), 1.66 (3H, br s, 10-H_3), 3.20 (3H, s, OCH_3), 3.82 (2H, d, J=7 Hz, 1-H_2), 5.03 (1H, m, 7-H), 5.23 (1H, t-like, 2-H). MS m/z(%): 168 (M^+, 17), 68 (100).

1-*O*-Methyl-10-hydroxygeraniol (5b) from 3b——A solution of **3b** (10.0 g, 59.5 mmol) in 95% EtOH (120 ml) and pyridine (5 ml) was treated with a solution of SeO_2 (6.7 g, 60.4 mmol) in 95% EtOH (60 ml) and the mixture was heated under reflux for 1 h. After partial removal of the solvent under reduced pressure from the yellow-green reaction mixture to leave a volume of *ca.* 20 ml, the residue was treated with ether (50 ml). The insoluble material was removed by filtration and the ethereal filtrate was washed successively with aq. sat. $NaHCO_3$, water, and aq. sat. NaCl, then dried over $MgSO_4$. The ethereal solution was concentrated to 50 ml and treated with MeOH (5 ml). The ice-cooled solution was treated dropwise with a suspension of $NaBH_4$ (3.0 g, 78.9 mmol) is ether–MeOH (10:1, 100 ml) during a period of 15 min and stirred for a further 15 min. The reaction mixture was then treated with aq. 5% HCl and extracted with EtOAc. Work-up of the EtOAc extract in the usual manner gave a light yellow product (11.3 g), which was purified by column chromatography (SiO_2 550 g, hexane : EtOAc = 5 : 1) to furnish 1-*O*-methyl-10-hydroxygeraniol (**5b**, 6.3 g, 58%). **5b**, colorless oil, bp 103—105 °C (3 mmHg). *Anal.* Calcd for $C_{11}H_{20}O_2$: C, 71.69; H, 10.94. Found: C, 71.61; H, 10.89. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3625, 3475 (br), 1670. ^1H NMR (δ): 1.61 (3H, br s, 9-H_3), 1.63 (3H, br s, 4-H_3), 2.83 (1H, br s, OH, exchangeable with D_2O), 3.22 (3H, s, OCH_3), 3.84 (2H, d, J=7 Hz, 1-H_2), 5.24 (2H, m, 2-H, 7-H). MS m/z(%): 184 (M^+, 1), 43 (100).

1-*O*-Acetyl-10-hydroxynerol (6a) from Nerol (2)——A solution of nerol (**2**, 10 g) in Ac_2O (10 ml) and pyridine (10 ml) was left standing at room temp. (25 °C) for 1.5 h. The reaction mixture was poured into ice-water and the whole was extracted with EtOAc. Work-up of the EtOAc extract as described above for the acetylation of geraniol gave a product which was purified by distillation under reduced pressure [bp 74—75 °C (1 mmHg)] to furnish neryl acetate (**4a**, 12.0 g). A solution of **4a** (10 g, 51.0 mmol) in 99% EtOH (200 ml) and pyridine (7.5 ml) was treated with SeO_2 (5.7 g, 51.3 mmol) and the whole mixture was heated under reflux for 1 h. The resulting yellow-green reaction mixture was concentrated under reduced pressure to a volume of *ca.* 20 ml and the residue was treated with ether (30 ml). After removal of the precipitate by filtration, the ethereal solution was washed with aq. sat. $NaHCO_3$ and aq. sat. NaCl, then dried over $MgSO_4$. The solvent was partly removed under reduced pressure to leave a volume of 150 ml, then the solution was diluted with MeOH (15 ml) and treated with $NaBH_4$ (3.0 g, 78.9 mmol) in small portions under ice-cooling with stirring for 1 h. The reaction mixture was then treated with aq. 5% HCl and extracted with ether. Work-up of the ether extract in the usual manner gave a brown product (11.0 g), which was purified by column chromatography (SiO_2 550 g, hexane : EtOAc = 5 : 1) to furnish 1-*O*-acetyl-10-hydroxynerol (**6a**, 6.9 g, 60% from **2**). **6a**, colorless oil. *Anal.* Calcd for $C_{12}H_{20}O_3$: C, 67.89; H, 9.50. Found: C, 68.03; H, 9.74. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3625, 3510 (br), 1745, 1670. ^1H NMR (δ): 1.60 (3H, br s, 9-H_3), 1.63 (3H, br s, 4-H_3), 2.83 (1H, br s, OH, exchangeable with D_2O), 3.86 (2H, br s, 10-H_2), 4.48 (2H, d, J=7 Hz, 1-H_2), 5.29 (2H, m, 2-H, 7-H). MS m/z(%): 152 (M^+ − AcOH, 6), 43 (100).

Neryl Methyl Ether (4b) from Nerol (2)——A solution of **2** (10.0 g) in DMSO (250 ml) was treated with a dimsyl carbanion DMSO solution (prepared as above) and the mixture was stirred at room temp. (25 °C) for 2 h. The ice-cooled reaction mixture was then treated with CH_3I (16 ml) and stirred at room temp. for 1 h. The reaction mixture was poured into ice-water and the whole was extracted with EtOAc. Work-up of the EtOAc extract as described above afforded a product (12.0 g), which was purified by distillation under reduced pressure to furnish neryl methyl ether (**4b**, 9.5 g, 87%). **4b**, colorless oil, bp 49—50 °C (1 mmHg). *Anal.* Calcd for $C_{11}H_{22}O$: C, 78.51; H, 11.98. Found: C, 78.32; H, 11.87. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1678. ^1H NMR (δ): 1.59 (3H, br s, 9-H_3), 1.66 (3H, br s, 4-H_3), 1.72 (3H, br s, 10-H_3), 3.20 (3H, s, OCH_3), 3.80 (2H, d, J=7 Hz, 1-H_2), 5.04 (1H, m, 7-H), 5.23 (1H, m, 2-H). MS m/z(%): 168 (M^+, 4), 93 (100).

1-*O*-Methyl-10-hydroxynerol (6b) from 4b——A solution of **4b** (4.4 g, 26 mmol) in 95% EtOH (60 ml)–pyridine (2.5 ml) was treated with SeO_2 (2.8 g, 25 mmol) and the mixture was heated under reflux for 1 h. After concentration of the yellow-green reaction mixture to a volume of *ca.* 8 ml under reduced pressure, the residue was treated with ether (25 ml). The resulting precipitate was removed by filtration and the ethereal solution was washed with aq. sat. $NaHCO_3$ and aq. sat. NaCl, then dried over $MgSO_4$. After partial removal of the solvent to leave a volume of 75 ml, the solution was diluted with MeOH (7.5 ml) and treated with $NaBH_4$ (1.2 g, 32 mmol) under ice-cooling with stirring for 1 h. Work-up of the reaction mixture as described above for the preparation of **5b** yielded a brownish oily product (5.2 g) which was purified by column chromatography (SiO_2 250 g, hexane : EtOAc = 5 : 1) to furnish 1-*O*-methyl-10-hydroxynerol (**6b**, 2.6 g, 54%). **6b**, colorless oil. *Anal.* Calcd for $C_{11}H_{20}O_2$: C, 71.69; H, 10.94. Found: C, 71.59; H, 10.93. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3620, 3460 (br), 1670. ^1H NMR (δ): 1.62 (3H, br s, 9-H_3), 1.64 (3H, br s, 4-H_3), 2.87 (1H, br s, OH, exchangeable with D_2O), 3.22 (3H, s, OCH_3), 3.83 (2H, d, J=7 Hz, 1-H_2), 3.83 (2H, br s, 10-H_2), 5.24 (2H, m, 2-H, 7-H). MS m/z(%): 184 (M^+, 1), 43 (100).

Formic Acid Treatment of 1-*O*-Acetyl-10-hydroxygeraniol (5a)——A solution of **5a** (215 mg) in 98% HCOOH (15 ml) was stirred at room temp. (20 °C) for 2 h, then treated with water (50 ml) and KOH (40 g) under ice-cooling, and the whole was stirred at room temp. for 1 h. The reaction mixture was extracted with EtOAc and the EtOAc extract was washed successively with aq. 1 N H_2SO_4, aq. sat. $NaHCO_3$, and aq. sat. NaCl, then dried over $MgSO_4$.

Removal of the solvent under reduced pressure furnished a light yellow oily product (200 mg), which was purified by column chromatography (SiO_2 20 g, hexane : EtOAc = 2 : 1) to furnish **7** (158 mg, 92%). **7**, colorless oil. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3400 (br), 1672. ^1H NMR (δ): 1.00 (3H × 3/5, s, 10-H_3), 1.03 (3H × 2/5, s, 10-H_3), 1.61 (3H, br s, 7-H_3), 3.40 (2H, m, 9-H_2), 4.02 (2H, br s, OH, exchangeable with D_2O), 5.29 (1H, m, 2-H). MS *m/z* (%): 170 (M^+, 1), 43 (100). High resolution MS *m/z*: Found 170.130. Calcd for $C_{10}H_{18}O_2$ (M^+) 170.131.

Formic Acid Treatment of 1-*O*-Acetyl-10-hydroxynerol (6a)——A solution of **6a** (60 mg) in 98% HCOOH (5 ml) was stirred at room temp. (20 °C) for 2 h. The reaction mixture was then treated with water (15 ml) and KOH (13 g) under ice-cooling and the mixture was stirred at room temp. for 30 min. The reaction mixture was extracted with EtOAc and the EtOAc extract was worked up as described above. A brown oily product (65 mg) obtained after work-up as described above was purified by column chromatography (SiO_2 6 g, hexane : EtOAc = 2 : 1) to furnish **7** (38 mg, 79%). The product obtained here was shown to be identical with **7** obtained above from **5a** by TLC (hexane : EtOAc = 2 : 1), IR (CCl_4), and ^1H NMR (CCl_4) comparisons.

Conversion of 7 to (±)-α-Terpineol (8)——A solution of **7** (144 mg) in pyridine (2 ml) was treated with *p*-TsCl (140 mg) and the mixture was allowed to stand at 30 °C overnight. The reaction mixture was poured into ice-water and the whole was extracted with EtOAc. The EtOAc extract was washed successively with aq. 5% HCl, aq. sat. $NaHCO_3$, and aq. sat. NaCl, then dried over $MgSO_4$. Removal of the solvent under reduced pressure afforded a monotosylate (231 mg), IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3500, 1598, 1370. A solution of the monotosylate (230 mg) in dry ether (5 ml) was treated with $LiAlH_4$ (12 mg) and the mixture was heated under reflux for 30 min. After cooling, the reaction was quenched with aq. ether and the mixture was acidified with aq. 5% HCl and extracted with ether. The ether extract was washed with aq. sat. $NaHCO_3$ and aq. sat. NaCl, and dried over $MgSO_4$. Removal of the solvent under reduced pressure furnished a colorless oily product (**8**, 86 mg, 78%), which was shown to be identical with authentic (±)-α-terpineol by TLC (hexane : EtOAc = 3 : 1), IR (film), and ^1H NMR (CCl_4) comparisons.

BF_3-Etherate Treatment of 1-*O*-Acetyl-10-hydroxygeraniol (5a)——Under an N_2 atmosphere, an ice-cooled stirred solution of **5a** (13.0 g, 6.1 mmol) in dry CH_2Cl_2 (150 ml) was treated dropwise with BF_3-etherate (5.0 ml, 40 mmol) during a period of 15 min, then the mixture was stirred under ice-cooling for 90 min. The reaction was quenched by adding aq. sat. $NaHCO_3$ and the whole was extracted with CH_2Cl_2. The CH_2Cl_2 extracted was washed with aq. sat. NaCl and dried over $MgSO_4$. Removal of the solvent under reduced pressure gave an orange oily product (1.42 g) which was purified by column chromatography (SiO_2 70 g, hexane : EtOAc = 60 : 1) to furnish P-1 (**9**, 46 mg, 5.2%), P-2 (**10**, 31 mg, 3.3%), P-3 (**17**, 165 mg, 17.7%), and P-4 (**24**, 20 mg, 2.1%). P-1 (**9**), colorless oil. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1675. ^1H NMR (δ): 1.00 (3H, d, J = 7 Hz, 8-H_3), 1.67 (3H, br s, 9-H_3), 3.10 (1H, dd, J = 7, 8 Hz, 2-H_A), 3.90 (1H, dd, J = 8, 8 Hz, 2-H_B), 4.10 (1H, t-like, 7a-H), 5.36 (1H, m, $W_{h/2}$ = 7 Hz, 7-H). ^{13}C NMR (δ_C): 17.54 (q, 8-C), 23.54 (q, 9-C), 23.83 (t, 4-C), 27.78 (t, 5-C), 37.38, 43.91 (both d, 3-C, 3a-C), 73.29 (t, 2-C), 74.46 (d, 7a-C), 122.26 (d, 7-C), 136.00 (s, 6-C). MS *m/z* (%): 152 (M^+, 17), 137 (100). High resolution MS *m/z*: Found 152.120. Calcd for $C_{10}H_{16}O$ (M^+) 152.120. P-2 (**10**), colorless oil. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1675. ^1H NMR (δ): 0.96 (3H, d, J = 7 Hz, 8-H_3), 1.70 (3H, br s, 9-H_3), 2.47 (1H, hep.-like, 3-H), 3.27 (1H, dd, J = 8, 9 Hz, 2-H_A), 3.78 (1H, dd, J = 8, 8 Hz, 2-H_B), 4.01 (1H, t-like, 7a-H), 5.46 (1H, m, $W_{h/2}$ = 8 Hz, 7-H). ^{13}C NMR (δ_C): 11.70 (q, 8-C), 19.10 (t, 4-C), 23.44 (q, 9-C), 29.58 (t, 5-C), 36.84, 40.10 (both d, 3-C, 3a-C), 71.58 (t, 2-C), 75.38 (d, 7a-C), 121.39 (d, 7-C), 137.27 (s, 6-C). MS *m/z* (%): 152 (M^+, 12), 137 (100). High resolution MS *m/z*: Found 152.118. Calcd for $C_{10}H_{16}O$ (M^+): 152.120. P-3 (**17**), colorless oil. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3630, 3590, 3480 (br), 1665. ^1H NMR (δ): 1.07 (3H, d, J = 7 Hz, 10-H_3), 1.72 (3H, br s, 9-H_3), 2.21 (2H, m, 1-H, 4-H_A), 3.69 (1H, dd, J = 4, 6 Hz, 7-H), 5.22 (1H, m, $W_{h/2}$ = 8 Hz, 3-H). ^{13}C NMR (δ_C): 20.32 (q, 10-C), 24.85 (q, 9-C), 30.01 (t, 8-C), 36.84 (t, 4-C), 40.20 (d, 5-C), 46.10, 47.56 (both d, 1-C, 6-C), 88.30 (d, 7-C), 118.75 (d, 3-C), 138.29 (s, 2-C). MS *m/z* (%): 152 (M^+, 6), 94 (100). High resolution MS *m/z*: 152.120. Calcd for $C_{10}H_{16}O$ (M^+): 152.120. P-4 (**24**), colorless oil. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3625, 3570, 3470 (br), 1660. ^1H NMR (δ): 0.88 (3H, d, J = 7 Hz, 10-H_3), 1.68 (3H, br s, 9-H_3), 4.16 (1H, dd, J = 6, 10 Hz, 7-H), 5.27 (1H, m, $W_{h/2}$ = 8 Hz, 3-H). ^{13}C NMR (δ_C): 11.40 (q, 10-C), 24.95 (q, 9-C), 28.99 (t, 8-C), 31.97 (t, 4-C), 37.08, 38.74 (both d, 5-C, 6-C), 45.32 (d, 1-C), 76.94 (d, 7-C), 120.07 (d, 3-C), 138.39 (s, 2-C). MS *m/z* (%): 152 (M^+, 3), 94 (100). High resolution MS *m/z*: Found 152.120. Calcd for $C_{10}H_{16}O$ (M^+): 152.120.

BF_3-Etherate Treatment of 1-*O*-Methyl-10-hydroxygeraniol (5b)——Under an N_2 atmosphere, an ice-cooled, stirred solution of **5b** (1.02 g, 5.54 mmol) in dry CH_2Cl_2 (200 ml) was treated dropwise with BF_3-etherate (5.0 ml, 40 mmol) during a period of 15 min, and the ice-cooled mixture was stirred for a further 90 min. The reaction was quenched by adding aq. sat. $NaHCO_3$ and the whole was extracted with CH_2Cl_2. Work-up of the CH_2Cl_2 extract as described above for **5a** gave an orange oily product (980 mg) which was purified by column chromatography (SiO_2 50 g, hexane : EtOAc = 60 : 1) to furnish P-1 (**9**, 96 mg, 11.4%), P-2 (**10**, 53 mg, 6.3%), P-3 (**17**, 195 mg, 23.1%), and P-4 (**24**, 16 mg, 1.9%).

BF_3-Etherate Treatment of 1-*O*-Acetyl-10-hydroxynerol (6a)——Under an N_2 atmosphere, an ice-cooled, stirred solution of **6a** (27 mg, 0.13 mmol) in dry CH_2Cl_2 (8 ml) was treated dropwise with BF_3-etherate (0.17 ml, 1.35 mmol), and the mixture was stirred under ice-cooling for 30 min. Work-up of the reaction mixture as described above for **5a** furnished an orange oily product (26 mg). The percentage composition of products (P-1, P-2, P-3, P-4, and others) was determined by GLC (given in Table I).

BF_3-Etherate Treatment of 1-*O*-Methyl-10-hydroxynerol (6b)——Treatment of **6b** (17 mg, 0.09 mmol) in dry

CH_2Cl_2 (5 ml) with BF_3-etherate (0.15 ml, 1.19 mmol) for 30 min and work-up of the reaction mixture as described for **6a** yielded an orange oily product (16 mg). The percentage composition of the products (P-1, P-2, P-3, and P-4) is given in Table I.

Catalytic Hydrogenation of P-1 (9)——A solution of **9** (360 mg) in 99% EtOH (40 ml) was treated with PtO_2 (100 mg) and the mixture was stirred vigorously under an H_2 atmosphere (1 atm) at room temp. (10 °C) for 10 h. After removal of the catalyst by filtration, the solvent was evaporated off under reduced pressure to yield an oily product (370 mg). Purification of the product by column chromatography (SiO_2 37 g, hexane : EtOAc = 10 : 1) furnished a dihydro derivative (**11**, 343 mg, 94%). **11**, colorless oil. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1025. ^1H NMR (δ): 0.88 (3H, d, J = 6 Hz, 9-H_3), 0.96 (3H, d, J = 7 Hz, 8-H_3), 2.10 (1H, hep.-like, 3-H), 3.20 (1H, dd, J = 8, 8 Hz, 2-H_A), 3.94 (1H, dd, J = 8, 8 Hz, 2-H_B), 3.7—4.1 (1H, m, 7a-H). MS m/z (%): 154 (M^+, 51), 69 (100). High resolution MS m/z: Found 154.135. Calcd for $C_{10}H_{18}O$ (M^+) 154.136.

RuO_2–$NaIO_4$ Oxidation of 11——A solution of **11** (210 mg) in CCl_4 (10 ml) was treated with $RuO_2 \cdot xH_2O$ (20 mg) and the resulting suspension was treated with a solution of $NaIO_4$ (2.0 g) in water (10 ml). The mixture was then stirred vigorously at room temp. (20 °C) for 20 h. The organic phase was separated and the aqueous phase was extracted with CH_2Cl_2. The combined organic phase and the CH_2Cl_2 extract was washed with water and treated with EtOH (2 ml). The precipitate (RuO_2) was removed by passing the mixture through a Celite 545 column. Removal of the solvent under reduced pressure from the filtrate gave a white solid (268 mg), which was purified by column chromatography (SiO_2 27 g, hexane : EtOAc = 10 : 1) to furnish a γ-lactone (**12**, 220 mg, 96%). **12**, colorless plates, mp 54.0—54.5 °C (hexane). *Anal.* Calcd for $C_{10}H_{16}O_2$: C, 71.39; H, 9.59. Found: C, 71.46; H, 9.55. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1785, 1170, 998. ^1H NMR (δ): 0.94 (3H, d, J = 6 Hz, 9-H_3), 1.12 (3H, d, J = 7 Hz, 8-H_3), 2.26 (1H, m, 3-H), 4.33 (1H, dt, J = 10, 6 Hz, 7a-H). MS m/z (%): 124 ($M^+ - CO_2$, 16), 81 (100).

Catalytic Hydrogenation of P-2 (10)——A solution of **10** (160 mg) in 99% EtOH (35 ml) was hydrogenated over PtO_2 (100 mg) and worked up as described above for **9**. Purification of the product (176 mg) by column chromatography (SiO_2 18 g, hexane : EtOAc = 10 : 1) furnished **13** (127 mg, 79%). **13**, colorless oil. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1035. ^1H NMR (δ): 0.95 (3H, d, J = 7 Hz, 8-H_3), 1.00 (3H, d, J = 6 Hz, 9-H_3), 2.33 (1H, hep.-like, 3-H), 3.31 (1H, dd, J = 8, 8 Hz, 2-H_A), 3.76 (1H, dd, J = 8, 8 Hz, 2-H_B), 3.86 (1H, dt, J = 5, 4 Hz, 7a-H). MS m/z (%): 154 (M^+, 90), 97 (100). High resolution MS m/z: Found 154.135. Calcd for $C_{10}H_{18}O$ (M^+) 154.136.

RuO_2–$NaIO_4$ Oxidation of 13——A solution of **13** (35 mg) in CCl_4 (2 ml) was treated with a RuO_4–CCl_4 solution (prepared from $RuO_2 \cdot xH_2O$ 300 mg, $NaIO_4$ 1.0 g, and CCl_4 10 ml) and the mixture was stirred vigorously at room temp. (20 °C) for 2.5 h. The reaction mixture was treated with EtOH (3 drops) and the precipitate (RuO_2) was removed with the aid of Celite 545. Work-up of the filtrate as described above for **11** gave a colorless oily product (36 mg), which was purified by column chromatography (SiO_2 4 g, hexane : EtOAc = 10 : 1) to furnish **14** (18 mg, 48%). **14**, colorless oil. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1777, 1156, 962. ^1H NMR (δ): 1.06 (3H, d, J = 6 Hz, 9-H_3), 1.12 (3H, d, J = 7 Hz, 8-H_3), 2.57 (1H, m, 3-H), 4.32 (1H, m, 7a-H). MS m/z (%): 168 (M^+, 1), 125 (100). High resolution MS m/z: Found 168.113. Calcd for $C_{10}H_{16}O_2$ (M^+) 168.115.

K_2CO_3 Treatment of 12——A solution of **12** (20 mg) in dry *m*-xylene (5 ml) was treated with dry K_2CO_3 (powder, 200 mg) and the mixture was heated under reflux under an N_2 atmosphere for 15 h. After the removal of K_2CO_3 by filtration, the solvent was evaporated off under reduced pressure from the filtrate to yield a colorless oily product (20 mg). The product was shown to be the unchanged starting compound (**12**) by GLC (15% PEGS, 3 mm × 3 m), IR (CCl_4), and ^1H NMR (CCl_4) comparisons.

K_2CO_3 Treatment of 14——A solution of **14** (5 mg) in dry *m*-xylene (2 ml) was treated with dry K_2CO_3 (powder, 50 mg) and the mixture was heated under reflux under an N_2 atmosphere for 5 h. Work-up of the reaction mixture as described above yielded a product (5 mg), which was shown to be identical with **12** by GLC, IR, and ^1H NMR comparisons as described above.

Conversion from γ-Lactone (12) to Butenolide (15)——Under an N_2 atmosphere, a solution of **12** (100 mg, 0.59 mmol) in dry THF (10 ml) was treated dropwise at −78°C with an LDA–THF solution (prepared from diisopropylamine 0.15 ml, 1.07 mmol, 15% *n*-BuLi in hexane 0.45 ml, 0.71 mmol, and dry THF 10 ml) during a period of 15 min. After being stirred at −78 °C for a further 3 h, the reaction mixture was treated with a solution of dimethyl disulfide (0.14 ml, 1.56 mmol) in dry THF (3 ml) and the mixture was stirred for 30 min. The reaction temperature was allowed to rise gradually to room temp. (21 °C) over 1 h and the mixture was treated with aq. sat. NH_4Cl then extracted with EtOAc. The EtOAc extract was washed with aq. sat. NaCl and dried over $MgSO_4$. Removal of the solvent under reduced pressure gave a light yellow product (128 mg). A solution of the product in CH_2Cl_2 (10 ml) was treated with a solution of $NaIO_4$ (300 mg, 1.40 mmol) in water (10 ml) and the mixture was stirred vigorously at room temp. for 35 min. The organic phase was taken and the aqueous phase was extracted with CH_2Cl_2. The combined organic phase and CH_2Cl_2 extract was washed with aq. 15% $Na_2S_2O_3$ and aq. sat. NaCl, then dried over $MgSO_4$. Removal of the solvent under reduced pressure gave a crude sulfoxide (174 mg). The sulfoxide, without purification, was dissolved in dry toluene (10 ml) and the solution was heated under reflux under an Ar atmosphere for 5 h. Removal of the solvent under reduced pressure gave a yellow oily product (135 mg), which was purified by column chromatography (SiO_2 15 g, hexane : EtOAc = 5 : 1) to furnish **15** (78 mg, 80% from **12**). **15**, colorless oil. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1770, 1695, 1032. UV λ_{max}^{EtOH} nm (ε): 217 (1.4×10^4).

^{1}H NMR (δ): 1.10 (3H, d, J=6 Hz, 9-H$_3$), 1.72 (3H, t, J=1 Hz, 8-H$_3$), 4.52 (1H, br dd, 7a-H). MS m/z(%): 166 (M^+, 100). High resolution MS m/z: Found 166.099. Calcd for $C_{10}H_{14}O_2$ (M^+) 166.099.

DIBAL Reduction of Butenolide (15) Giving (±)-Menthofuran (16)——A solution of **15** (28 mg) in dry THF (2 ml) was treated at −23 °C under an Ar atmosphere with a 1.16 N DIBAL–THF solution (0.50 ml) and the mixture was stirred for 20 h. The reaction mixture was acidified with aq. 10% H_2SO_4 and extracted with EtOAc. The EtOAc extract was washed with aq. sat. $NaHCO_3$ and aq. sat. NaCl, then dried over $MgSO_4$. Removal of the solvent under reduced pressure gave a colorless oily product (29 mg), which was purified by column chromatography (SiO_2 5 g, hexane) to furnish **16** (20 mg, 77%). **16** was shown to be identical with authentic (+)-menthofuran by TLC (hexane, detection with the Ehrlich reagent), GLC (HB-2000, 0.25 mm × 45 m), IR (CCl_4), and ^{1}H NMR (CCl_4) comparisons.

Acetylation of P-3 (17)——A solution of **17** (90 mg) in dry pyridine (5 ml) was treated with Ac_2O (5 ml) and the mixture was left standing at room temp. (20 °C) for 2 d. The reaction mixture was poured into ice-water and the whole was extracted with EtOAc. Work-up of the EtOAc extract in the usual manner gave a monoacetate (**18**, 114 mg, 99%). **18**, colorless oil. *Anal.* Calcd for $C_{12}H_{18}O_2$: C, 74.19; H, 9.34. Found: C, 73.88; H, 9.28. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1745, 1248, 1038. ^{1}H NMR (δ): 1.08 (3H, d, J=7 Hz, 10-H$_3$), 1.58 (3H, br s, 9-H$_3$), 1.96 (3H, s, OAc), 4.62 (1H, dd, J=4, 5 Hz, 7 H), 5.15 (1H, m, $W_{h/2}$=8 Hz, 3-H). MS m/z(%): 194 (M^+, 9), 93 (100).

Ozone Oxidation of 18——A solution of **18** (55 mg) in MeOH (7 ml) was bubbled through ozonized oxygen at −78 °C for 30 min. The cooled solution was then bubbled through with nitrogen to remove excess ozone. After warming to room temp. (22 °C), the reaction mixture was treated with AcOH (0.5 ml) and Zn powder (15 mg) and the whole was stirred for 40 min. The MeOH was removed by distillation under reduced pressure and the residue was treated with EtOAc. After removal of the insoluble material by filtration, the filtrate was washed with aq. sat. $NaHCO_3$ and aq. sat. NaCl, then dried over $MgSO_4$. Removal of the solvent under reduced pressure furnished a keto-aldehyde (**19**, 60 mg, 95%). **19**, colorless oil. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 2820, 2720, 1740, 1730. ^{1}H NMR (δ): 1.04 (3H, d, J=7 Hz, 10-H$_3$), 1.96, 2.03 (3H each, both s, COCH$_3$, OAc), 2.53 (2H, m, 4-H$_2$), 3.16 (1H, m, 1-H), 4.91 (1H, dd, J=4, 7 Hz, 7-H), 9.88 (1H, t, J=2 Hz, CHO). MS m/z(%): 166 (M^+ − AcOH, 2), 43 (100). High resolution MS m/z: Found 226.121. Calcd for $C_{12}H_{18}O_4$ (M^+) 226.121.

Methylation of P-3 (17)——A solution of **17** (100 mg) in dry DME (1 ml) was added to a suspension of NaH (35 mg) in dry DME (2 ml) under an N_2 atmosphere, and the mixture was stirred at room temp. (25 °C) for 1.5 h. After treatment with CH_3I (0.5 ml), the reaction mixture was stirred at 65—75 °C for 3 h. The reaction mixture was then poured into ice-water and the whole was extracted with EtOAc. The EtOAc extract was washed with aq. 15% $Na_2S_2O_3$ and aq. sat. NaCl, then dried over $MgSO_4$. Removal of the solvent under reduced pressure gave a light yellow product (113 mg), which was purified by column chromatography (SiO_2 15 g, hexane : EtOAc = 10 : 1) to furnish a monomethyl ether (**20**, 98 mg, 89%). **20**, colorless oil. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1670, 1110. ^{1}H NMR (δ): 1.11 (3H, d, J=7 Hz, 10-H$_3$), 1.73 (3H, br s, 9-H$_3$), 3.3—3.5 (1H, m, 7-H), 3.40 (3H, s, OCH$_3$), 5.27 (1H, m, 3-H). MS m/z(%): 166 (M^+, 24), 94 (100). High resolution MS m/z: Found 166.136. Calcd for $C_{11}H_{18}O$ (M^+) 166.136.

Hydroboration–Oxidation of 20——A stirred solution of **20** (50 mg) and $NaBH_4$ (10 mg) in dry THF (2 ml) was treated dropwise at room temp. (23 °C) with a BF_3-etherate–THF solution (1 : 1, 0.10 ml) during a period of 1 h. After being stirred for a further 2 h, the reaction mixture was treated with water (1 ml), aq. 3 N NaOH (0.5 ml), and aq. 30% H_2O_2 (0.5 ml) and the whole was stirred at 23—43 °C for 1.5 h. The reaction mixture was then treated with aq. sat. NaCl and extracted with EtOAc. The EtOAc extract was washed successively with aq. 5% HCl, aq. sat. $NaHCO_3$, and aq. sat. NaCl, then dried over $MgSO_4$. The product (60 mg) obtained by removal of the solvent under reduced pressure was dissolved in CH_2Cl_2 (2 ml) and the solution was treated with PCC (80 mg) under an N_2 atmosphere. The reaction mixture was stirred at room temp. (25 °C) for 2 h, diluted with dry ether (5 ml) and passed through a Florisil column. Removal of the solvent under reduced pressure from the eluate gave a colorless oily product (61 mg), which was purified by column chromatography (SiO_2 6 g, hexane–EtOAc = 5 : 1) to furnish **21** (45 mg, 83%). **21**, colorless oil. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1720, 1107. ^{1}H NMR (δ): 1.08 (3H, d, J=7 Hz, 10-H$_3$), 1.22 (3H, d, J=6 Hz, 9-H$_3$), 3.2—3.5 (1H, m, 7-H), 3.28 (3H, s, OCH$_3$). MS m/z(%): 182 (M^+, 7), 83 (100). High resolution MS m/z: Found 182.130. Calcd for $C_{11}H_{18}O_2$ (M^+) 182.131.

PCC Oxidation of P-3 (17)——A suspension of PCC (213 mg) in CH_2Cl_2 (2 ml) was treated with a solution of **17** (100 mg) in CH_2Cl_2 (2 ml) and the mixture was stirred at room temp. (20 °C) for 2.5 h. The reaction mixture was diluted with dry ether (10 ml) and passed through a Florisil column to remove the precipitate. Removal of the solvent under reduced pressure from the filtrate gave an oily product (98 mg), which was purified by column chromatography (SiO_2 10 g, hexane : EtOAc = 20 : 1) to furnish **22** (85 mg, 86%). **22**, colorless oil. *Anal.* Calcd for $C_{10}H_{14}O$: C, 79.95; H, 9.39. Found: C, 79.56; H, 9.64. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1743. ^{1}H NMR (δ): 1.00 (3H, d, J=8 Hz, 10-H$_3$), 1.69 (3H, br s, 9-H$_3$), 5.27 (1H, m, 3-H). MS m/z(%): 150 (M^+, 4), 93 (100).

$NaBH_4$ Reduction of 22 Reverting P-3 (17)——A solution of **22** (10 mg) in ether–MeOH (10 : 1, 4 ml) was treated with $NaBH_4$ (3 mg) under ice-cooling. After warming to room temp. (20 °C), the reaction mixture was stirred for 30 min. The mixture was treated with aq. 5% HCl (2 drops) and extracted with EtOAc. The EtOAc extract was washed with aq. sat. $NaHCO_3$ and aq. sat. NaCl, then dried over $MgSO_4$. Removal of the solvent under reduced pressure furnished **17** (10 mg, 99%), which was shown to be identical with authentic P-3 by TLC (hexane : EtOAc =

5:1), GLC (HB-2000, 0.25 mm × 45 m), IR (CCl_4), and ^1H NMR (CCl_4) comparisons.

Isomerization from 22 to 23——Under an N_2 atmosphere, a solution of **22** (100 mg, 0.67 mmol) in dry THF (1 ml) was treated dropwise at −78 °C with an LDA–THF solution (prepared from diisopropylamine 0.20 ml, 1.43 mmol, 15% *n*-BuLi in hexane 0.50 ml, 0.80 mmol, and dry THF 2 ml) during a period of 5 min. The temperature of the reaction mixture was gradually raised to −10 °C over 1 h. The reaction mixture was then treated with AcOH (0.085 ml, 1.34 mmol) and stirred for 2 min. After warming to room temp. (20 °C), the reaction mixture was treated with aq. sat. NH_4Cl. The organic phase was separated, washed with aq. sat. NaCl and dried over $MgSO_4$. Removal of the solvent under reduced pressure gave a colorless oily product (100 mg), which was purified by column chromatography (SiO_2 15 g, hexane: EtOAc = 30:1) to furnish **22** (6 mg, 6% recovery) and **23** (84 mg, 84%). **23**, colorless oil. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1738. ^1H NMR (δ): 1.06 (3H, d, J = 7 Hz, 10-H_3), 1.68 (3H, br s, 9-H_3), 5.26 (1H, m, 3-H). MS *m/z* (%): 150 (M^+, 33), 93 (100). High resolution MS *m/z*: Found 150.105. Calcd for $C_{10}H_{14}O$ (M^+) 150.104.

$NaBH_4$ Reduction of 23 Giving P-4 (24)——A solution of **23** (45 mg) in ether–MeOH (10:1, 10 ml) was treated with $NaBH_4$ (12 mg) under ice-cooling. After warming to room temp. (20 °C), the mixture was stirred for 30 min, treated with aq. 5% HCl and extracted with EtOAc. Work-up of the EtOAc extract as described above for **22** gave a product (47 mg, 99%) which was shown to be identical with P-4 (**24**) by TLC (hexane: EtOAc = 5:1), GLC (HB-2000, 0.25 mm × 45 m), IR (CCl_4), and ^1H NMR (CCl_4) comparisons.

OsO_4 Oxidation of 22——A solution of **22** (100 mg) in dry pyridine (1.5 ml) was treated with OsO_4 (190 mg) and the mixture was stirred at room temp. (25 °C) for 16 h. The reaction mixture was then treated with a solution of $NaHSO_3$ (300 mg) in water (1.5 ml)–pyridine (1.0 ml), and the whole was stirred for 2 h, poured into ice-water and extracted with $CHCl_3$. The $CHCl_3$ extract was washed successively with aq. 5% HCl, aq. sat. $NaHCO_3$, and aq. sat. NaCl, then dried over $MgSO_4$. Removal of the solvent under reduced pressure gave a white solid (120 mg) which was purified by column chromatography (SiO_2 10 g, hexane: EtOAc = 1:1) to furnish **25** (110 mg, 90%). **25**, colorless needles, mp 148—150 °C (benzene: EtOH = 4:1). IR $\nu_{max}^{CH_2Cl_2}$ cm^{-1}: 3590, 3550, 1740, 1068, 987. ^1H NMR ($CDCl_3$: CD_3OD = 15:85, with a trace amount of CF_3COOH, δ): 1.09 (3H, d, J = 7 Hz, 10-H_3), 1.26 (3H, s, 9-H_3), 3.32 (1H, dd, J = 6, 10 Hz, 3-H). MS *m/z* (%): 184 (M^+, 16), 43 (100). High resolution MS *m/z*: Found 184.109. Calcd for $C_{10}H_{16}O_3$ (M^+) 184.110. These physical data are in good accord with the data reported by Larsen and Monti.[17]

OsO_4 Oxidation of 23——A solution of **23** (100 mg) in dry pyridine (1.5 ml) was treated with OsO_4 (190 mg) and the mixture was stirred at room temp. (25 °C) for 21 h. The reaction mixture was then treated with a solution of $NaHSO_3$ (300 mg) in water (1.5 ml)–pyridine (1.0 ml) and the whole was stirred for a further 2 h. Work-up of the reaction mixture as described for **22** gave a white solid (123 mg), which was purified by column chromatography (SiO_2 10 g, hexane: EtOAc = 1:1) to furnish **26** (106 mg, 88%). **26**, colorless needles, mp 124—125 °C (benzene: EtOH = 4:1). IR $\nu_{max}^{CH_2Cl_2}$ cm^{-1}: 3595, 3550, 1736, 1055, 988. ^1H NMR ($CDCl_3$: CD_3OD = 15:85, with a trace amount of CF_3COOH, δ): 1.09 (3H, d, J = 7 Hz, 10-H_3), 1.26 (3H, s, 9-H_3), 3.11 (1H, dd, J = 6, 10 Hz, 3-H). MS *m/z* (%): 184 (M^+, 11), 43 (100). High resolution MS *m/z*: Found 184.109. Calcd for $C_{10}H_{16}O_3$ (M^+) 184.110.

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