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Studies on Terpenoids and Related Alicyclic Compounds. XVII.[1] Total Syntheses of Sesquiterpenoids; (±)-Isopetasol, (±)-3-Epiisopetasol, (±)-Warburgiadione, and (±)-Petasitol

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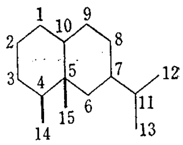
The total syntheses of (±)-isopetasol (**24**), (±)-3-epiisopetasol (**17**), (±)-warburgiadione (**23**), (±)-petasitol (**27a**) are described. A key intermediate (**11**) was synthesized by the Robinson annulation of 2,3-dimethylcyclohexane-1,4-dione (**6**), which was prepared starting from 2,3-dimethylphenol (**2**) and methyl vinyl ketone *via* intermediates **8** and **9**. Reduction of **11** with $NaBH_4$ gave epimeric alcohols (**13a** and **14a**) in the 7 : 3 ratio. Stereochemistry of **13a** and **14a** and the coresponding acetates (**13b** and **14b**) were confirmed by NMR spectrometry. Introduction of the C-7 side chain in **13a** was made with CH_3Li to give **16** which was treated with HCl–MeOH to afford (±)-**17**. While, the same procedure applied to **14a** was unsucessful. Ketal (**19**) derived from **11** was converted to isopropyl alcohol (**21**) by two routes. Treatment of **21** with HCl–MeOH gave (±)-isopetasone (**22**). (±)-**23** and (±)-**24** were obtained from **22** by dehydrogenation and reduction, respectively. Dehydrogenation of **21** by 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) gave a cross dienone (**25**). Deketalization of **25** followed by reduction afforded (±)-**27a** and (±)-3-epipetasitol (**28**).

Keywords——total synthesis; sesquiterpenoid; eremophilanes; isopetasol; warburgiadione; petasitol; 2,3-dimethylcyclohexane-1,4-dione; Robinson annulation; aldol-retroaldol condensation

Butterbus ("Fuki" in Japanese) are widely distributed in this country, and they have been used as foods and drugs. The structural elucidations of the components of these *Petasites* in Compositae have extensively been studied by several groups. Now many kinds of eremophilane type sesquiterpenoids have been isolated and structures determined.[3]

The eremophilane type sesquiterpenoids (**1**) are characterized by a framework which does not obey the well known isoprene rule. Eremophilanes have interesting aspect from a synthetic standpoint, namely the vicinal *cis*-4,5-dimethyl substituents on the hydronaphthalene framework. In this paper, we wish to report in detail the total syntheses of (±)-isopetasol, (±)-3-epiisopetasol, (±)-warburgiadione, and (±)-petasitol.



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Synthesis of a Bicyclic Key Intermediate (11)

A bicyclic key intermediate (**11**) was synthesized by the Robinson annulation[4] of 2,3-dimethylcyclohexane-1,4-dione (**6**) and methyl vinyl ketone. The starting material, 2,3-dimethylcyclohexane-1,4-dione (**6**), was prepared starting from 2,3-dimethylphenol (**2**) by the following procedure. Oxidation of **2** with Fremy's salt[5] gave 2,3-dimethyl-*p*-quinone (**3**)

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[1] Total syntheses of (±)-isopetasol, (±)-3-epiisopetasol, and (±)-warburgiadione have been reported as a preliminary communication [K. Yamakawa, I. Izuta, H. Oka, and R. Sakaguchi, *Tetrahedron Lett.*, **1974**, 2187]. Part XVI. K. Yamakawa and T. Satoh, *Chem. Pharm. Bull.* (Tokyo), **26**, 3704 (1978).

[2] Location: *12-Ichigaya-funagawara-machi, Shinjuku-ku, Tokyo 162, Japan.*

[3] T.K. Devon and A.I. Scott, "Handbook of Naturally Occurring Compounds" Vol. II, Academic Press, New York 1972, pp. 129—134; A.R. Pinder, *Fortschr. Chem. Org. Naturst.*, 34, 81 (1977).

[4] M.E. Jung, *Tetrahedron*, 32, 3 (1976); R.E. Gawley, *Synthesis*, **1976**, 777.

[5] W. Moser and R.A. Howie, *J. Chem. Soc.* (*A*), **1968**, 3039.

which was then reduced with aqueous sodium hydrosulfite to afford 2,3-dimethyl-*p*-hydroquinone (**4**), mp 163—164°, in 46% yield from **2**. Catalytic reduction of **4** with Raney nickel under 130 atm at 160° gave an isomeric mixture of 2,3-dimethyl-1,4-dihydroxycyclohexane (**5**) as a viscous oil, from which one isomer was crystallized from benzene to afford colorless needles, mp 104—106°. Oxidation of the diol (**5**) with Jones reagent gave a stereoisomeric mixture of 2,3-dimethylcyclohexane-1,4-dione (**6**) in 58% yield from **4**, which crystallized in part as mp 66—68°.

Condensation of diketone (**6**) and methyl vinyl ketone in the presence of sodium ethoxide at −20° for 2 days was carried out. The reaction products were chromatographed on silica gel to give three intermediates; (**7**) mp 92—94°, (**8**) mp 145—146°, and (**9**) mp 163—166°, in a ratio of 1:1:0.05. The structures of **7**, **8**, and **9** were determined by their spectral data and chemical transformations.[1]

Mass spectra of compounds **7**, **8**, and **9** showed the same molecular ion at *m/e* 210 for their molecular formula $C_{12}H_{18}O_3$. Compound (**7**) showed an absorption band at 1710 cm^{-1}

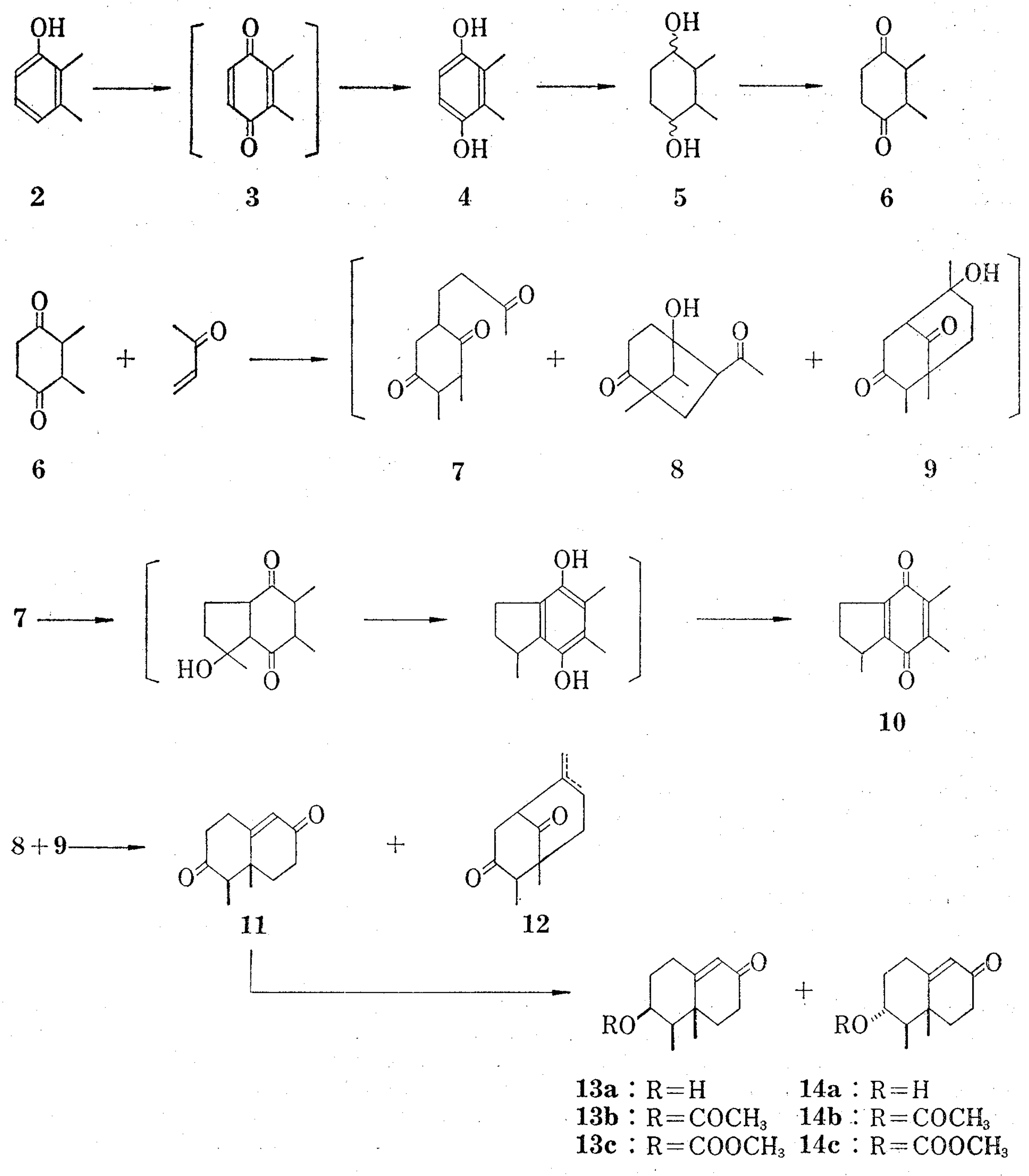

Chart 1

for carbonyl group in its infrared (IR) spectrum and showed characteristic signals at δ 1.15 (d, J=7 Hz, 2- and 3-CH_3) and 2.12 (s, $COCH_3$) in its nuclear magnetic resonance (NMR) spectrum. Treatment of **7** with *p*-toluenesulfonic acid in refluxing benzene for 24 hr gave a quinone (**10**), mp 35—36.5°, *via* a hydroquinone derivative which was formed by intramolecular cyclization and aromatization. From the spectral data and chemical evidence, the structure of **7** should be shown as a Michael adduct 2,3-dimethyl-6-(3′-oxobutyl)cyclohexane-1,4-dione.

Compound **8** showed absorption bands at 3400 cm^{-1} for hydroxyl group and at 1710 and 1705 cm^{-1} for carbonyl groups in its IR spectrum and showed signals at δ 0.82 (d, J=7.5 Hz, CH_3), 1.03 (s, CH_3), and 2.24 (s, $COCH_3$) in its NMR spectrum. The third compound (**9**) showed absorption bands at 3420 and 1710 cm^{-1} in its IR spectrum and also showed signals at δ 1.11 (s, CH_3), 1.14 (d, J=7.5 Hz, CH_3), 1.37 (s, CH_3), and 2.12 (s, OH) in its NMR spectrum.

Treatment of **8** and **9** with *p*-toluenesulfonic acid in refluxing benzene for 24 hr gave an enone (**11**), mp 101—103° in 53% yield together with a mixture of olefins (**12**) in 2% yield. From the above spectral data and chemical fact, the structures of **8** and **9** should be shown to be 6-acetyl-5-hydroxy-1,8-dimethyl-bicyclo[3.2.1]octan-2-one and 6-hydroxy-1,2,6-trimethyl-bicyclo[3.3.1]nonane-3,9-dione, respectively. Since the enone (**11**) is presumed to possess C-4 methyl group with more stable equatorial (β) orientation due to enolization of 3-oxo group, the enone (**11**) may be formulated with *cis*-vicinal 4,5-dimethyl configuration. This bicyclic enone (**11**) is an important key intermediate toward the total syntheses of sesquiterpenes of eremophilane–valencane family.

Selective reduction of the 3-oxo group of **11** with sodium borohydride in ethanol was carried out. The reduction product was chromatographed on silica gel to afford isomeric alcohols (**13a** and **14a**) as oily products in a 7:3 ratio. Since the hydride reagent is considered to attack favorably from α-side due to steric hindrance, the reduction of **11** should furnish predominantly 3β(axial)-ol (**13a**). The stereochemistry of epimeric alcohols (**13a** and **14a**) and corresponding acetates (**13b** and **14b**) were confirmed by their NMR spectra. The proton on C-3 attached with hydroxyl group in **13a** and **14a** appeared as quartet-like signals ($W_{1/2}$ =7.5 Hz at δ 3.94) and double triplet-like signals (J=4.5 and 10 Hz, $W_{1/2}$=25 Hz at δ 3.55), respectively. Furthermore, the signal due to C-5 angular methyl group of the acetate (**13b**) mp 71—72° shifted to upper field (*ca.* 2—3 Hz) than that of **13a**. The acetylation effect would be explained by the Kawazoe rule.[6] On comparison of the NMR spectra of **14a** and **14b**, the signal due to angular methyl group of **14b** shifted to lower field (8 Hz) than that of **14a**. This NMR data showed lack of the acetylation effect between the angular methyl and the C-3 acetoxyl group of **14b**. Based on the finding mentioned above, the hydroxyl group of **13a** is presumed to possess axial configuration, whereas **14a** possesses equatorial configuration. The half height band width ($W_{1/2}$) of axial or equatorial C-3 proton is expected to be over 12 Hz or below 9 Hz, respectively, as reported by Kawazoe *et al.*[6] The $W_{1/2}$ value of **13a, b** and **14a, b** are observed as 7.5 Hz and 25 Hz, respectively, thus supporting the above conclusion. Consequently, the configuration of hydroxyl groups of **13a** and **14a** were confirmed as β-axial and α-equatorial, respectively.

Djerassi *et al.*[7] obtained (+)-3α-hydroxy-4β,5β-dimethyloctalin-9-en-8-one (**14a**) from (+)-isopetasol (**24**) by the base-catalyzed retro-aldol reaction. IR and ultraviolet (UV) spectral data of (±)-**14a** were in good agreement with those of the natural compound. Consequently, the stereoformula of **14a** was confirmed.

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[6] Y. Kawazoe, Y. Sato, M. Natsume, H. Hasegawa, T. Okamoto, and K. Tsuda, *Chem. Pharm. Bull.* (Tokyo), **10**, 338 (1962).

[7] A. Aebi and C. Djerassi, *Helv. Chim. Acta*, **42**, 1785 (1959); D. Herbst and C. Djerassi, *J. Am. Chem. Soc.*, **82**, 4337 (1960).

Synthesis of (±)-3-Epiisopetasol (17)

Introductions of the side chain at C-7 position in enones (**13a** and **14a**) toward syntheses of 3-epiisopetasol (**17**) and isopetasol (**24**) were investigated. Treatment of **13a**, the major alcohol, with dimethyl carbonate in the presence of sodium hydride gave a mixture of diester (**15**), mp 127.5—128.5°, and a minor product O-monoester (**13c**), mp 113—114.5°. In the NMR spectrum of **15**, a signal due to a proton at C-7 is observed as a double doublet at δ 3.50. From this fact, the configuration of 7-methoxycarbonyl group of **15** was confirmed as α-equatorial. Methylation of **15** by treatment with an equivalent of sodium hydride and an excess of methyl lithium gave an isopropyl derivative (**16**), mp 168—169°, quantitatively. The structure of **16** was confirmed by the NMR spectrum which showed a singlet signal at δ 1.21 ascribable to *gem*-dimethyl protons and by disappearance of the ester carbonyl absorption band in the IR spectrum. Treatment of **16** with a catalytic amount of hydrochloric acid in refluxing methanol afforded an isopropylidene compound, (±)-3-epiisopetasol (**17**), mp 109—110°, in 78% yield together with a small amount of enone (**13a**) which was formed *via* a retro-aldol cleavage.

Next, for the purpose of total synthesis of (±)-isopetasol (24), the similar procedure was applied to the minor enone alcohol (**14a**). However, treatment of **14a** with two equivalents of sodium hydride followed by addition of an excess amount of dimethyl carbonate gave only a mixture of a monoester (**14c**), mp 79—81°, and an oily compound (**18**), but the desired diester could not be detected. Therefore, total synthesis of (±)-isopetasol by this route was abandoned.

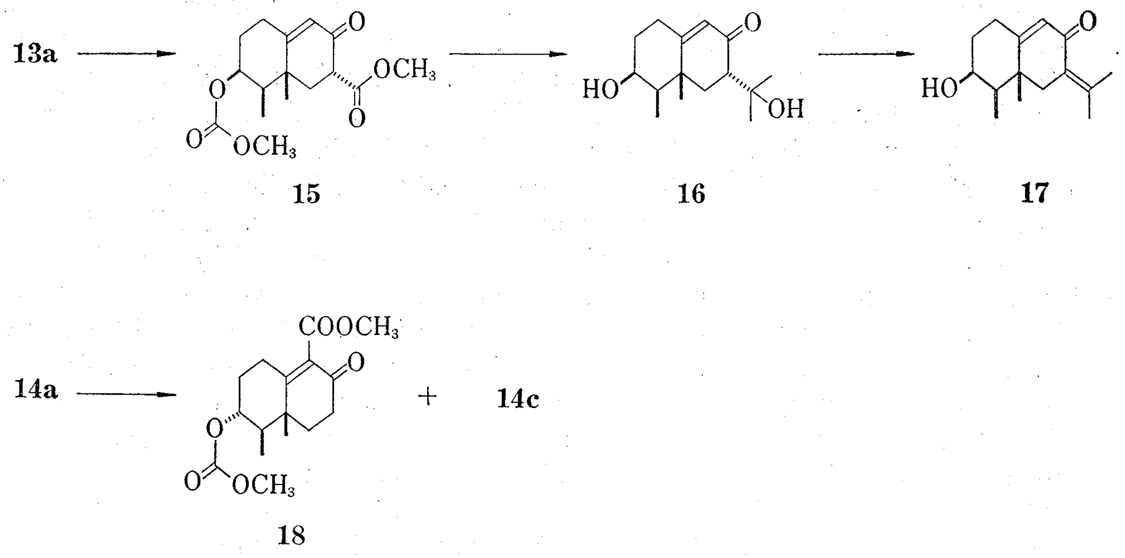

Chart 2

Synthesis of (±)-Warburgiadione (23) and (±)-Isopetasol (24)

Heating under reflux of the enone (**11**) with ethylene glycol in benzene containing a catalytic amount of *p*-toluenesulfonic acid gave a monoketal compound (**19**), mp 80—82°. In order to introduce a side chain at 7-position of **19**, **19** was treated with dimethyl carbonate in the presence of sodium hydride in absolute dioxane to give an enone ester (**20a**), mp 158—160°, in good yield. The NMR spectrum of **20a** showed a one-proton signal at δ 3.50 (dd, J=6, 11 Hz for 7-H), so the introduced methoxycarbonyl substituent should be assigned as having α-equatorial orientation.[8]

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[8] The C-7 side chain of **20** and **21** has equatorial α-configuration and not β as erroneously reported in the preliminary communication.[1]

Methylation of **20a** with an excess amount of ethereal methyl lithium in the presence of sodium hydride afforded isopropyl alcohol (**21**), mp 101°. **21** showed hydroxyl absorption band and the signal due to *gem*-dimethyl group at C-11 in its IR and NMR spectra, respectively. An alternative synthesis of the alcohol (**21**) through condensation of the enone (**19**) with acetone was also investigated.[9] Treatment of **19** with lithium diisopropylamide followed by condensation with acetone in the presence of zinc chloride gave the alcohol (**21**), mp 101°, in 77% yield.

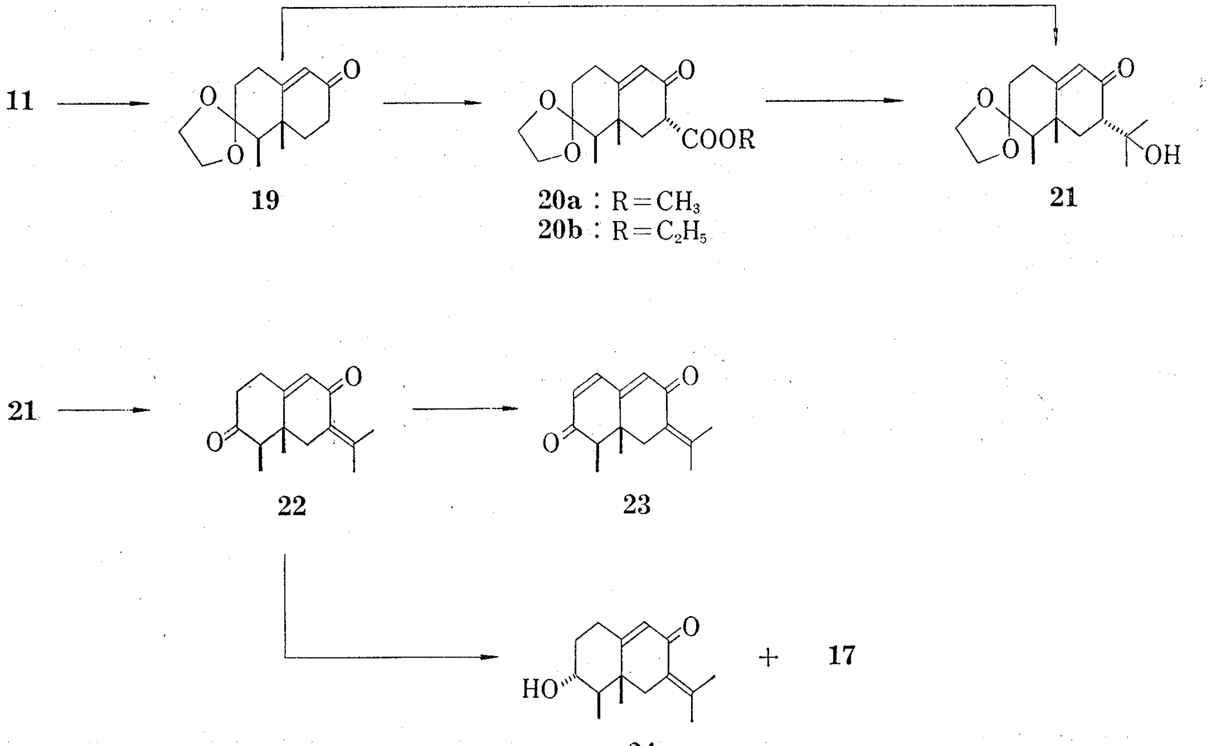

Chart 3

Dehydration and deketalization of **21** with a catalytic amount of hydrochloric acid in refluxing methanol produced a keto-isopropylidene derivative (**22**), mp 110—112°. The NMR data of (±)-**22** was in good agreement with that of isopetasone derived from isopetasol by Kurihara *et al.*[10] Treatment of **22** with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) in dioxane furnished (±)-warburgiadione (**23**), mp. 84—87°. IR and NMR spectra of (±)-**23** were identical with those of warburgiadione which was isolated from the heartwood of *Warburgia ugandensis* Sprague (Canellaceae) reported by Brooks and Draffan.[11]

Reduction of **22** with sodium borohydride gave (±)-isopetasol (**24**), mp 105—106°, and (±)-3-epiisopetasol (**17**), mp 109—110°, in a ratio of 1:5. IR, UV, NMR spectra and gas and thin-layer chromatographic data confirmed the identity of (±)-**24** with (+)-isopetasol which was isolated from *Petasites japonicus* Maxim by Naya *et al.*[12] The stereoformula of the epimeric alcohol (**17**) was also confirmed to be (±)-3-epiisopetasol.

Synthesis of (±)-Petasitol (27a)

Recently, Naya *et al.*[13] have isolated a new eremophilane sesquiterpenoid, petasitin (**27b**) from *Petasites japonicus* Maxim as the main component and reported the structural

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[9] The authors thank to Professor Torii, Okayama University, informed to us for this procedure.

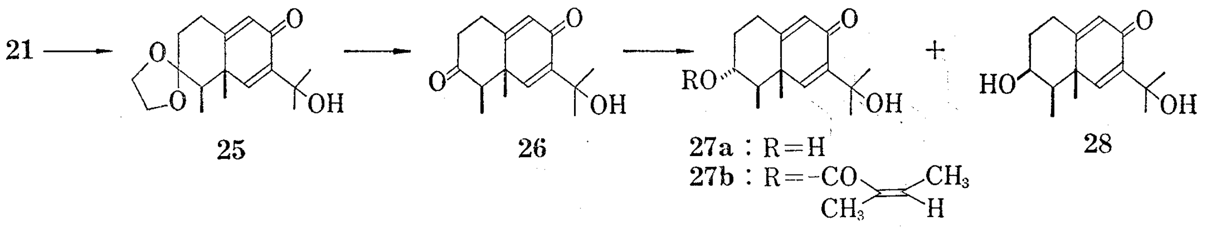
[10] T. Kurihara, K. Ro, H. Takada, H. Ito, *Tohoku Yakka Daigaku Nenpo*, **13**, 75 (1960).

[11] C.J.W. Brooks and G.H. Draffan, *Chem. Commun.*, **1966**, 701.

[12] K. Naya, I. Takagi, Y. Kawaguchi, and Y. Asada, *Tetrahedron*, **24**, 5871 (1968).

determination. The structure of petasitin (**27b**) was established from spectral data and chemical transformations. Petasitin has a characteristic cross dienone moiety as a typical eudesmane sesquiterpenoid santonin.

Very recently, Naya *et al.*[13b] reported the conversion of isopetasin into petasitin (**27b**) by photosensitized oxygenation. However, total synthesis of (±)-petasitin has not yet been achieved. We will report here a total synthesis of (±)-petasitol (**27a**) starting from the alcohol (**21**). Treatment of **21** with DDQ in refluxing dioxane for 24 hr afforded 6,9-dien-8-one (**25**), mp 110—111°, in 55.4% yield. UV spectrum of **25** showed λ maximum at 244 nm which indicated the presence of a cross 6,9-dien-8-one moiety rather than a 1,9-dien-8-one system. After deketalization of **25**, reduction of resulting 6,9-diene-3,8-dione (**26**) with sodium borohydride at 0° gave a mixture of epimeric alcohols (**27a** and **28**). Separation of the crude alcohol by preparative thin-layer chromatography (TLC) gave (±)-petasitol (**27a**) as oil and (±)-3-epipetasitol (**28**), mp 132—133°, in 15% and 77% yield, respectively. IR, UV, and NMR spectra of **27a** were in good agreement with those of (−)-petasitol derived from (−)-petasitin isolated from *Petasites japonicus* Maxim by Naya *et al.*[13b] The epimeric alcohol (**28**) was also confirmed to be 3β-hydroxyl compound by its physico-chemical data.



25 26 27a : R=H 28

27b : R=-CO(CH₃)C=C(CH₃)H

Chart 4

Experimental

All melting points are uncorrected. IR spectra were recorded for KBr disk with Hitachi 215 and Hitachi Perkin-Elmer 225 spectrophotometers. UV spectra were measured with Hitachi 323 and 200 spectrophotometers. NMR spectra were taken for solution in $CDCl_3$ unless otherwise cited and they were measured with JEOL JNM-4H-100 and JNM-FX-100 at 100 MHz spectrometers using Me_4Si as the internal standard. Mass spectra (MS) were recorded on a Hitachi RMU-7M double focusing mass spectrometer connected with a Hitachi data lyser 002 system at 70 eV by using direct insertion. Wako silica gel C-200 containing 2% fluorescent reagent 254 and quartz column were used for column chromatography. Preparative TLC was carried out using Merck silica gel HF_{254}.

2,3-Dimethylhydroquinone (4)——To a solution of freshly prepared 100 g of Fremy's salt (prepared from 69 g of $NaNO_2$ and 70 g of $NaHSO_3$), and 109 g of NaOAc in 800 ml of water was added dropwise a solution of 10 g of 2,3-dimethylphenol (2) in 10 ml of MeOH at 0° with stirring. The reaction mixture was vigorously stirred at 0° for 2 hr and then the reaction temperature was slowly elevated to room temperature. After the reaction was completed, the mixture was saturated with NaCl. The precipitate was filtered out, the filtrate was extracted with ether and the ether layer was shaken with sat. $Na_2S_2O_4$, washed, and dried. Removal of ether left 5.2 g of 2,3-dimethylhydroquinone (**4**), in 46% yield from **2**. Recrystallization from MeOH gave pure **4** as colorless needles, mp 163—164°. IR cm^{-1}: 3250 (OH). NMR δ: 1.65 (6H, s, 2- and 3-CH_3), 6.00 (2H, s, 5- and 6-H), 6.85 (2H, s, 1- and 4-OH).

2,3-Dimethylcyclohexane-1,4-dione (6)——Catalytic reduction of 4 (50 g) in 250 ml of EtOH with W-6 Raney nickel (25 g) at 150° under H_2 atmosphere of 140 kg/cm^2 was carried out. The nickel catalyst was removed and then EtOH was evaporated to afford diol (**5**), quantitatively, as viscous oil which was partially crystallized. Recrystallization from benzene gave colorless needles, mp 104—106°. IR cm^{-1}: 3350 (OH), 975, 950 (C–OH). NMR δ: 0.99 (6H, d, $J=7$ Hz, 2- and 3-CH_3), 1.48 (2H, s, 1- and 4-OH), 3.85 (2H, m, 1- and 4-H).

To a stirring solution of diol (**5**) in ether (1250 ml) in an ice bath was added dropwise 200 ml of Jones reagent (CrO_3, 70 g). After completion of the reaction, MeOH was added into the mixture for decomposition

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13) *a*) K. Naya and I. Takagi, *Tetrahedron Lett.*, **1968**, 629; *b*) I. Takagi, Y. Tazuke, and K. Naya, *Bull. Chem. Soc. Jpn.*, **50**, 3320 (1977).

of the excess oxidant. The ether layer was successively washed with sat. $NaHCO_3$, sat. NaCl, and dried. Evaporation of ether gave 35 g of brown oily compound, which was distilled under reduced pressure, $bp_{9.6}$ 110°, to give pale yellow oil (29.4 g; 58% yield), which was partially crystallized. Recrystallization from benzene–hexane gave **6** as colorless rhombic plates, mp 66—68°. *Anal.* Calcd. for $C_8H_{12}O_2$: C, 68.53; H, 8.64. Found: C, 68.78; H, 8.40. IR cm^{-1}: 1715 (CO). NMR δ: 1.24 (6H, d, $J=7$ Hz, 2- and 3-CH_3), 2.47 (2H, m, 2- and 3-H), 2.78 (4H, s, 5- and 6-H).

Condensation of Diketone (6) and Methyl Vinyl Ketone——(a) To a stirring solution of diketone (**6**) (14.0 g; 0.1 mol) in abs. EtOH (175 ml) at −20° under N_2 stream was added NaOEt (Na 70 mg in 1 ml of abs. EtOH). Freshly distilled methyl vinyl ketone 8.0 g (0.11 mol) was added dropwise to the mixture at −20° and stirring was continued at the same temperature for 2 days. H_2O (30 ml) was added to the reaction mixture. After evaporation of the solvent *in vacuo*, the residue was extracted with ether, washed and dried. Removal of ether gave the residue which was distilled to give two fractions of bp_4 92—94° (4.31 g; recovery of crude diketone) and bp_3 158—160° (10.56 g; 50% yield of adduct fraction). The viscous adduct fraction was chromatographed on silica gel to give three bands 1—3 in a ratio of 1: 1: 0.05.

Band 1: Elution with benzene, and recrystallization from benzene–hexane gave 2,3-dimethyl-6-(3′-oxobutyl)cyclohexane-1,4-dione (**7**) as colorless needles, mp 92—94°. *Anal.* Calcd. for $C_{12}H_{18}O_3$: C, 68.54; H, 8.63. Found: C, 68.54; H, 8.61. IR cm^{-1}: 1710 (CO). NMR δ: 1.15 (6H, d, $J=7$ Hz, 2- and 3-CH_3), 2.12 (3H, s, $COCH_3$).

Band 2: Elution with benzene–EtOAc (10: 1), and recrystallization from benzene gave 6-acetyl-5-hydroxy-1,8-dimethyl-bicyclo[3.2.1]octan-2-one (**8**), mp 145—146°, as colorless prisms. *Anal.* Calcd. for $C_{12}H_{18}O_3$: C, 68.54; H, 8.63. Found: C, 68.54; H, 8.61. IR cm^{-1}: 3400 (OH), 1710, 1705 (CO). NMR δ: 0.82 (3H, d, $J=7.5$ Hz, 8-CH_3), 1.03 (3H, s, 5-CH_3), 2.24 (3H, s, 7-$COCH_3$).

Band 3: Elution with benzene–EtOAc (10: 1) gave 6-hydroxy-1,2,6-trimethyl-bicyclo[3.3.1]nonane-3,9-dione (**9**). Recrystallization from benzene gave colorless crystals, mp 163—166°. *Anal.* Calcd. for $C_{12}H_{18}O_3$: C, 68.54; H, 8.63. Found: C, 68.77; H, 8.85. IR cm^{-1}: 3420 (OH), 1710 (CO). NMR δ: 1.11 (3H, s, 5-CH_3), 1.14 (3H, d, $J=7.5$ Hz, 4-CH_3), 1.37 (3H, s, 8-CH_3), 2.12 (1H, s, 8-OH).

Treatment of the Intermediates (7, 8, and 9) with *p*-Toluenesulfonic Acid——(a) The adduct (**7**) (100 mg), *p*-toluenesulfonic acid monohydrate (10 mg), and benzene (20 ml) were placed in a flask equipped with a Dean–Stark trap. The solution was refluxed for 24 hr. Ether (10 ml) was added to the reaction mixture and the organic layer was washed with sat. $NaHCO_3$, sat. NaCl, and dried. Removal of the solvent left a viscous oil which was purified by preparative TLC to afford a quinone (**10**), mp 33—35° (16 mg; 18% yield). Recrystallization from hexane gave yellow needles, mp 35—36.5°. High-resolution mass spectrum for $C_{12}H_{14}O_2$: Mol. Wt. 190.0992. Observed: M^+, 190.0979. IR cm^{-1}: 1635 (CO), 1605 (C=C). NMR δ: 1.20 (3H, d, $J=7$ Hz), 2.00 (6H, s).

(b) A solution of the adducts (a mixture of **8** and **9**) (1.20 g) and *p*-toluenesulfonic acid monohydrate (120 mg) in benzene (50 ml) was refluxed under the same conditions as described for **7**. After work-up, the viscous oily residue (1.2 g) was column chromatographed on silica gel. Elution with hexane–EtOAc gave 580 mg (53% yield) of enone (**11**) and 25 mg of a mixture of olefins (**12**). Recrystallization from benzene–hexane gave **11** as colorless needles, mp 101—103°. *Anal.* Calcd. for $C_{12}H_{16}O_2$: C, 74.97; H, 8.39. Found: C, 74.67; H, 8.66. IR cm^{-1}: 1710, 1670 (CO), 1620 (C=C). UV λ_{max}^{EtOH} 234 nm (ε 9500). NMR δ: 1.04 (3H, d, $J=7.5$ Hz, 4-CH_3), 1.07 (3H, s, 5-CH_3), 5.87 (1H, s, 9-H).

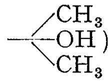
(±)-5β,6β-Dimethyl-2,7-dioxo-$\Delta^{1(10)}$-octalin (11)——The procedure was essentially under the same conditions described above for the condensation of **6** and methyl vinyl ketone except for purification of the intermediates. Diketone (**6**) (14 g) and methyl vinyl ketone (10.5 g) were added to a solution of EtONa–EtOH (prepared from 70 mg of Na and 175 ml of abs. EtOH) with stirring at −20° and the mixture was allowed to stand at the same temperature for 2 days. After work-up, the residue was chromatographed on silica gel. Elution with hexane–EtOAc (2: 1) gave the Michael adduct (8.9 g). The crude adduct was treated with *p*-toluenesulfonic acid in refluxing benzene for 24 hr to give 3.75 g of crude product. Column chromatography on silica gel and recrystallization from EtOAc–hexane afforded 2.16 g (11% yield from **6**) of **11** as colorless needles, mp 101—103°.

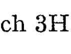
Reduction of Diketone (11) with $NaBH_4$——To an EtOH solution (50 ml) of **11** (1.0 g) was added $NaBH_4$ (76 mg) with stirring at 0°. A small amount of AcOH was added to the reaction mixture and then the solvent was evaporated *in vacuo*. The residue was extracted with ether, washed, and dried. After removal of solvent, the residue was column chromatographed on silica gel. Elution with hexane–EtOAc (5: 1) gave 3β-ol (**13a**) (700 mg; 70% yield) as oil, and elution with hexane–EtOAc (3: 1) gave 3α-ol (**14a**) (300 mg; 30% yield), as oil. 3β-ol (**13a**): IR cm^{-1}: 3450 (OH), 1670 (CO), 1620 (C=C). UV λ_{max}^{EtOH} 234 nm. NMR δ: 1.08 (3H, d, $J=7.5$ Hz, 4-CH_3), 1.33 (3H, s, 5-CH_3), 3.94 (1H, m, $W_{1/2}=7.5$ Hz, 3-H), 5.90 (1H, s, 9-H). 3α-ol (**14a**): IR cm^{-1}: 3450 (OH), 1680 (CO), 1620 (C=C). UV λ_{max}^{EtOH} 235 nm. NMR δ: 1.02 (3H, d, $J=7$ Hz, 4-CH_3), 1.12 (3H, s, 5-CH_3), 2.90 (1H, bs, OH), 3.55 (1H, m, $W_{1/2}=25$ Hz, 3-H), 5.75 (1H, s, 9-H).

3β-Ol (**13a**) (20 mg) was converted with Ac_2O–pyridine to the corresponding acetate (**13b**) (23 mg; 95% yield). Recrystallization from hexane gave colorless prisms, mp 71—72°. IR cm^{-1}: 1730, 1665 (CO), 1615 (C=C). NMR δ: 0.98 (3H, d, $J=7.5$ Hz, 4-CH_3), 1.29 (3H, s, 5-CH_3), 2.11 (3H, s, 3-$OCOCH_3$), 5.08 (1H, m, $W_{1/2}=7.5$ Hz, 3-H), 5.80 (1H, s, 9-H).

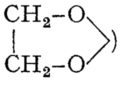
Treatment of 3α-ol (**14a**) in the same manner gave the corresponding acetate (**14b**) as oil. IR cm^{-1}: 1740, 1680 (CO), 1630 (C=C). NMR δ: 0.95 (3H, d, $J=7.5$ Hz, 4-CH_3), 1.18 (3H, s, 5-CH_3), 2.08 (3H, s, 3-$OCOCH_3$), 4.88 (1H, m, $W_{1/2}=25$ Hz, 3-H), 5.80 (1H, s, 9-H).

Reaction of 13a and Dimethyl Carbonate——A solution of **13a** (100 mg) in dioxane (5 ml) was added dropwise to a stirring suspension of NaH (50% in paraffin, 50 mg) in dioxane and then the mixture was added with an excess amount of dimethyl carbonate. The mixture was heated at 100° for 3 hr. 10% AcOH was added to the reaction mixture until the solution was neutralized, and the mixture was extracted with ether. The ether layer was washed with sat. $NaHCO_3$, sat. NaCl, and dried. Evaporation of ether gave an oily product which was chromatographed on silica gel. Elution with hexane–EtOAc (5:1) gave 100 mg (62% yield) of diester (**15**) and 50 mg (38% yield) of monoester (**13c**). Diester (**15**): Recrystallization from EtOH gave colorless prisms, mp 127.5—128.5°. *Anal.* Calcd. for $C_{16}H_{22}O_6$: C, 61.92; H, 7.15. Found: C, 61.79; H, 7.22. IR cm^{-1}: 1750, 1670 (CO), 1620 (C=C). NMR δ: 1.06 (3H, d, $J=7.5$ Hz, 4-CH_3), 1.33 (3H, s, 5-CH_3), 3.50 (1H, dd, $J=6$, 11 Hz, 7-H), 3.78 and 3.80 (each 3H, s, $COOCH_3$), 4.93 (1H, m, $W_{1/2}=$ 7.5 Hz, 3-H), 5.85 (1H, s, 9-H). Monoester (**13c**): Recrystallization from benzene–hexane gave colorless prisms, mp 113—114.5°. *Anal.* Calcd. for $C_{14}H_{20}O_4$: C, 66.64; H, 7.99. Found: C, 66.71; H, 7.97. IR cm^{-1}: 1745, 1675 (CO), 1620 (C=C). NMR δ: 1.05 (3H, d, $J=7.5$ Hz, 4-CH_3), 1.27 (3H, s, 5-CH_3), 3.78 (3H, s, $COOCH_3$), 4.91 (1H, m, $W_{1/2}=7.5$ Hz, 3-H), 5.80 (1H, s, 9-H).

3β,11-Dihydroxyeremophilan-9-en-8-one (16)——A solution of **15** (100 mg) in ether (2 ml) was added dropwise to a stirring suspension of NaH (50% in paraffin, 19 mg) in ether (5 ml) in an ice bath and then the mixture was added with an ether solution of an excess amount of CH_3Li. The reaction mixture was poured into ice-water and was extracted with ether and the ether solution was washed and dried. Removal of ether gave 114 mg of an oily product which was purified by preparative TLC to afford **16** (80 mg; 98% yield). Recrystallization from benzene–hexane gave colorless crystal, mp 168—169°. *Anal.* Calcd. for $C_{15}H_{24}O_3$: C, 71.39; H, 9.59. Found: C, 71.58; H, 9.66. IR cm^{-1}: 3420, 3370 (OH), 1645 (CO), 1630 (C=C). NMR δ: 1.10 (3H, d, $J=7.5$ Hz, 4-CH_3), 1.21 (6H, s,  $-C(OH)(CH_3)_2$), 1.45 (3H, s, 5-CH_3), 3.94 (1H, m, $W_{1/2}=7.5$ Hz, 3-H), 5.78 (1H, s, 9-H).

(±)-**3-Epiisopetasol (17)**——A solution of **16** (40 mg) in MeOH (10 ml) containing a catalytic amount of conc. HCl was refluxed for 3 hr. Evaporation of solvent *in vacuo* left a residue which was extracted with ether to give 42 mg of an oily product. Separation of the residue by preparative TLC developed with benzene–EtOAc (5:1) gave 29 mg (78% yield) of (±)-3-epiisopetasol (**17**) together with 10 mg of ketone (**13a**). Recrystallization of **17** from benzene–hexane gave colorless crystals, mp 109—110°. *Anal.* Calcd. for $C_{15}H_{22}O_2$: C, 76.88; H, 9.46. Found: C, 76.66; H, 9.56. IR cm^{-1}: 3530 (OH), 1660 (CO), 1630, 1610 (C=C). UV λ_{max}^{EtOH} nm (ε): 248 (11200), 279 (7000). NMR δ: 1.13 (3H, d, $J=7.5$ Hz, 4-CH_3), 1.18 (3H, s, 5-CH_3), 1.85 and 2.10 (each 3H, s,  $=C(CH_3)_2$), 3.95 (1H, m, 3-H), 5.80 (1H, s, 9-H). MS m/e: 234 (M^+).

Reaction of 14a and Dimethyl Carbonate——A solution of **14a** (100 mg) in dioxane (5 ml) was added dropwise to a stirring suspension of NaH (50 mg; 50% in paraffin) in dioxane and then the mixture was added with excess dimethyl carbonate. The mixture was heated at 100° for 3 hr. Work-up as described above gave the oily product which was separated by column chromatography on silica gel. Elution with hexane–EtOAc (5:1) gave **18** (95 mg; 62% yield) as oil and ester (**14c**) (40 mg; 32% yield). **14c**: Recrystallization from benzene–hexane gave colorless crystals, mp 79—81°. IR cm^{-1}: 1740, 1675 (CO), 1620 (C=C). NMR δ: 1.05 (3H, d, $J=7.5$ Hz, 4-CH_3), 1.20 (3H, s, 5-CH_3), 3.80 (3H, s, $COOCH_3$), 4.65 (1H, m, $W_{1/2}=$ 25 Hz, 3-H), 5.80 (1H, s, 9-H). **18**: IR (neat) cm^{-1}: 1740, 1670 (CO), 1620 (C=C). NMR δ: 1.10 (3H, d, $J=$ 7.5 Hz, 4-CH_3), 1.32 (3H, s, 5-CH_3), 3.80 (6H, s, $COOCH_3$).

3,3-Ethylenedioxy-4β,5β-dimethyloctalin-9-en-8-one (19)——A solution of diketone (**11**) (452 mg), *p*-toluenesulfonic acid monohydrate (60 mg), and ethylene glycol (175 mg) in benzene (50 ml) was refluxed for 8 hr. The reaction mixture was cooled to room temperature and was added with 50 ml of ether. The ether layer was washed with sat. $NaHCO_3$, sat. NaCl, and dried. Evaporation of solvent gave a reddish-brown oily product which was chromatographed on Florisil. Elution with hexane–EtOAc (10:1) gave ketal (**19**) (400 mg; 72% yield) and elution with hexane–EtOAc (3:1) gave recovered 40 mg of **11**. Recrystallization of **19** from hexane–benzene gave colorless needles, mp 80—82°. *Anal.* Calcd. for $C_{14}H_{20}O_3$: C, 71.16; H, 8.53. Found: C, 71.07; H, 8.77. IR cm^{-1}: 1670 (CO), 1620 (C=C), 1073 (C–O–C). UV λ_{max}^{EtOH} 236 nm (ε 10700). NMR δ: 0.93 (3H, d, $J=7.5$ Hz, 4-CH_3), 1.24 (3H, s, 5-CH_3), 4.00 (4H, m,  $\begin{matrix}CH_2\text{–}O\\|\\CH_2\text{–}O\end{matrix}\!\!>$), 5.77 (1H, s, 9-H). MS m/e (rel. intensity %): 236 (M^+, 23), 99 (100), 96 (82).

Methyl 3,3-Ethylenedioxy-8-oxo-4β,5β-dimethyloctalin-9-en-7-carboxylate (20a)——A dioxane (5 ml) solution of **19** (100 ml) was added dropwise to a stirring suspension of NaH (50% in paraffin, 41 mg) and an excess amount of dimethyl carbonate and the mixture was heated at 100° for 3 hr. AcOH was added to the reaction mixture until the solution was neutralized and the mixture was extracted with ether, washed, and dried. Evaporation of ether gave an oily product which was chromatographed on Florisil, eluted with hexane–EtOAc (10: 1) to afford methyl ester (**20a**) (120 mg; 96% yield). Recrystallization from EtOH gave colorless prisms, mp 158—160°. *Anal.* Calcd. for $C_{16}H_{22}O_5$: C, 65.29; H, 7.53. Found: C, 65.30; H, 7.63. IR cm^{-1}: 1745, 1670 (CO), 1630 (C=C). UV λ_{max}^{EtOH} 237 nm. NMR δ: 0.93 (3H, d, J=7.5 Hz, 4-CH_3), 1.26 (3H, s, 5-CH_3), 3.50 (1H, dd, J=6, 11 Hz, 7-H), 3.75 (3H, d, $COOCH_3$), 3.95 (4H, m, $\begin{matrix}CH_2-O\\|\\CH_2-O\end{matrix}\rangle$), 5.80 (1H, s, 9-H).

When diethyl carbonate was used for the above reaction, ethyl ester (**20b**), mp 125—129°, was obtained in 95% yield. *Anal.* Calcd. for $C_{17}H_{24}O_5$: C, 76.88; H, 9.46. Found: C, 76.57; H, 9.51. IR cm^{-1}: 1740, 1670 (CO), 1620 (C=C). UV λ_{max}^{EtOH} 238 nm. NMR δ: 0.95 (3H, s, J=7.5 Hz, 4-CH_3), 1.30 (3H, s, 5-CH_3), 1.30 (3H, t, J=7 Hz, $CO_2CH_2\underline{CH_3}$), 4.00 (4H, m, $\begin{matrix}CH_2-O\\|\\CH_2-O\end{matrix}\rangle$), 4.25 (2H, q, J=7 Hz, $CO_2\underline{CH_2}CH_3$), 5.80 (1H, s, 9-H).

3,3-Ethylenedioxy-11-hydroxyeremophil-9-en-8-one (21)——(a) From **20a** and **20b**: A solution of **20a** (200 mg) in ether (4 ml) was added dropwise to a stirring suspension of NaH (50% in paraffin, 33 mg) in an ice bath and then ether solution of an excess amount of CH_3Li was added to the reaction mixture. The reaction mixture was poured into ice-water and the mixture was extracted with ether, washed, and dried. Removal of ether gave an oily product which was chromatographed on silica gel to afford 180 mg (90% yield) of **21**. Recrystallization from EtOAc–hexane gave colorless needles, mp 101°. *Anal.* Calcd. for $C_{17}H_{26}O_4$: C, 69.34; H, 8.90. Found: C, 69.28; H, 8.88. IR cm^{-1}: 3460 (OH), 1650 (CO), 1625 (C=C). UV λ_{max}^{EtOH} 239 nm (ε 16000). NMR δ: 0.95 (3H, d, J=7 Hz, 4-CH_3), 1.22 (6H, s, $-\!\!\left\langle\begin{matrix}CH_3\\OH\\CH_3\end{matrix}\right.$), 1.28 (3H, s, 5-$CH_3$), 3.98 (4H, m, $\begin{matrix}CH_2-O\\|\\CH_2-O\end{matrix}\rangle$), 5.72 (1H, d, J=3 Hz, 9-H). MS m/e (rel. intensity %): 294 (M^+, 5), 174 (100), 99 (90).

The alcohol (**21**) was also prepared from **20b** (200 mg) to give 160 mg of **21** (87% yield).

(b) Condensation of **19** and Acetone: To a stirring solution of lithium diisopropylamide (prepared from 4 ml of 1.56 M butyl lithium in hexane and 1 ml of diisopropylamine) at −78° under N_2 stream was added dropwise a solution of **19** (300 mg) in dry THF (2 ml) during 1 hr. After stirring for 1 hr at the same temperature, a solution of $ZnCl_2$ (173 mg) in dry ether (1.8 ml) was added with stirring at 0° for 10 min. To this mixture dry acetone (1 ml) was added and the mixture was stirred at 0° for 5 min. The mixture was quenched with sat. NH_4Cl and extracted with ether, washed, and dried. Evaporation of ether gave an oily product which was purified by preparative TLC (developed with $CHCl_3$–EtOAc 5: 1) to afford 289 mg (77% yield) of **21**, as colorless needles, mp 101°.

(±)-Isopetasone (22)——A MeOH (10 ml) solution of **21** (100 mg) in the presence of a small amount of conc. HCl was refluxed for 3 hr. The mixture was concentrated *in vacuo*, and was extracted with ether. The ether layer was washed with sat. $NaHCO_3$, sat. NaCl, and dried. Removal of ether gave an oily product which was separated by preparative TLC (developed with benzene–EtOAc 5: 1) to afford (±)-isopetasone (**22**) (60 mg; 76% yield) together with enone (**11**). Recrystallization of **22** from benzene–hexane gave colorless prisms, mp 110—112°. *Anal.* Calcd. for $C_{15}H_{20}O_2$: C, 77.55; H, 8.68. Found: C, 77.42; H, 8.64. IR cm^{-1}: 1720, 1680 (CO), 1640, 1630 (C=C). NMR δ: 0.95 (3H, s, 5-CH_3), 1.08 (3H, d, J=7.5 Hz, 4-CH_3), 1.85 and 2.13 (each 3H, s, $=\!\left\langle\begin{matrix}CH_3\\CH_3\end{matrix}\right.$), 5.93 (1H, s, 9-H). The IR and NMR spectra of **22** were identified with those of isopetasone reported by Kurihara *et al.*[10] and Brooks and Draffan.[11]

Reduction of (±)-Isopetasone (22) with $NaBH_4$——To a stirring EtOH (10 ml) solution of (±)-isopetasone (**22**) (76 mg) was added $NaBH_4$ (4.9 mg) at 0°. A small amount of AcOH was added to the mixture and then EtOH was concentrated *in vacuo*. The residue was extracted with ether, washed, and dried. Removal of ether gave an oily product which was separated by preparative TLC. Development with benzene–EtOAc (5: 1) gave two bands 1 and 2.

Band 1: Recrystallization from benzene–hexane gave colorless needles of (±)-3-epiisopetasol (**17**) (48 mg; 63% yield), mp 109—110°. IR, NMR, and chromatographic data confirmed the identity with synthetic (±)-**17** described above.

Band 2: Recrystallization from benzene–hexane gave (±)-isopetasol (**24**) (10 mg; 15% yield), mp 105—106°. *Anal.* Calcd. for $C_{15}H_{22}O_2$: C, 76.88; H, 9.46. Found: C, 76.57; H, 9.51. IR cm^{-1}: 3430 (OH), 1660 (CO), 1630, 1610 (C=C). UV λ_{max}^{EtOH} nm (ε): 247 (12000), 279 (7200). NMR δ: 0.98 (3H, s, 5-CH_3), 1.10 (3H, d, J=7.5 Hz, 4-CH_3), 1.85 and 2.10 (each 3H, s, $=\!\left\langle\begin{matrix}CH_3\\CH_3\end{matrix}\right.$), 3.58 (1H, m, $W_{1/2}$=25 Hz, 3-H), 5.78 (1H, s, 9-H). MS m/e 234 (M^+). IR and NMR spectra of **24** were in good agreement with those of (+)-isopetasol reported by Naya *et al.*[12]

(±)-Warburgiadione (23)——A dioxane (4 ml) solution of (±)-**22** (37 mg), DDQ (45.4 mg), and catalytic amount of *p*-toluenesulfonic acid was refluxed for 2 hr. After the reaction was completed, the mixture was extracted with ether and then ether layer was washed with sat. $NaHCO_3$, sat. NaCl, and dried. Removal of ether gave an oily product, which was purified by preparative TLC to afford 10 mg (27% yield) of (±)-warburgiadione (**23**), mp 84—87° (from EtOAc–hexane), as yellow prisms. High-resolution mass spectrum for $C_{15}H_{18}O_2$: Mol. Wt. 230.1307. Observed: M^+ 230.1305. IR (CCl_4) cm^{-1}: 1690, 1670 (CO), 1620 (C=C). UV λ_{max}^{EtOH} 292 nm (ε 22200). NMR δ: 0.98 (3H, s, 5-CH_3), 1.16 (3H, d, J=7.5 Hz, 4-CH_3), 1.88 (3H, d, J=1.3 Hz, 13-CH_3), 2.16 (3H, d, J=2 Hz, 12-CH_3), 6.08 (1H, s, 9-H), 6.22 (1H, d, J=10 Hz, 2-H), 7.00 (1H, d, J=10 Hz, 1-H). IR and NMR spectra of **23** were in good agreement with those of (+)-warburgiadione reported by Brooks and Draffan.[11)]

3,3-Ethylenedioxy-11-hydroxyeremophila-6,9-dien-8-one (25)——A solution of **21** (110 mg) and DDQ (100 mg) in abs. dioxane (5 ml) was refluxed for 24 hr. The mixture was extracted with ether, washed, and dried. Removal of ether gave a brown oily product which was purified by preparative TLC developed with hexane–EtOAc (2:1) to afford 60.5 mg (55.4% yield) of crude dienone (**25**). Recrystallization from EtOAc–hexane gave **25** as colorless needles, mp 110—111°. *Anal.* Calcd. for $C_{17}H_{24}O_4$: C, 69.84; H, 8.27. Found: C, 69.84; H, 8.45. IR cm^{-1}: 3450 (OH), 1665 (CO), 1630 (C=C), 1070 (C–O–C). UV λ_{max}^{EtOH} 244 nm (ε 14000). NMR δ: 1.08 (3H, d, J=7 Hz, 4-CH_3), 1.28 (3H, s, 5-CH_3), 1.46 (6H, s, $-\!\!<\!\begin{smallmatrix}CH_3\\OH\\CH_3\end{smallmatrix}$), 3.96 (4H, m, $\begin{smallmatrix}CH_2-O\\|\\CH_2-O\end{smallmatrix}\!>$), 6.07 (1H, d, J=1.5 Hz, 9-H), 6.88 (1H, s, 6-H). MS *m/e* (rel. intensity %): 292 (M^+, 13), 277 (100).

11-Hydroxyeremophila-6,9-dien-3,8-dione (26)——**25** (60.5 mg) was dissolved in 70% AcOH (5 ml) and allowed to stand with stirring at room temperature for 7 days. Evaporation of solvent gave an oily product which was purified by preparative TLC developed with hexane–EtOAc (1:1) to afford dienone (**26**) (40 mg; 78% yield), as oil. IR ($CHCl_3$) cm^{-1}: 3480 (OH), 1715, 1660 (CO), 1620 (C=C). UV λ_{max}^{EtOH} 242 nm. NMR δ: 1.15 (3H, s, 5-CH_3), 1.20 (3H, d, J=7 Hz, 4-CH_3), 1.49 (6H, s, $-\!\!<\!\begin{smallmatrix}CH_3\\OH\\CH_3\end{smallmatrix}$), 6.13 (1H, m, 9-H), 6.83 (1H, s, 6-H). MS *m/e* (rel. intensity %): 248 (M^+, 10), 233 (72), 191 (100).

Reduction of 26 with $NaBH_4$——To a stirring EtOH solution (5 ml) of diketone (**26**) (90 mg) was added $NaBH_4$ (6 mg) at 0° and stirring was continued for 10 min. NH_4Cl was added to the mixture and the solution was concentrated *in vacuo*. The residue was extracted with ether, washed, and dried. Evaporation of ether gave an oily product which was separated by preparative TLC developed with hexane-EtOAc (2:1) to afford two bands 1 and 2. Band 1 and 2 gave 14 mg (15% yield) of (±)-petasitol (**27a**), oil, and 70 mg (77% yield) of (±)-3-epipetasitol (**28**), mp 132—133°, respectively. (±)-Petasitol (**27a**): High-resolution mass spectrum for $C_{15}H_{22}O_3$: Mol. Wt. 250.1570. Observed: M^+ 250.1593. IR cm^{-1}: 3450 (OH), 1660 (CO), 1615 (C=C). UV λ_{max}^{EtOH} 244 nm. NMR δ: 1.16—1.27 (6H, 4- and 5-CH_3), 1.47 (6H, s, $-\!\!<\!\begin{smallmatrix}CH_3\\OH\\CH_3\end{smallmatrix}$), 3.65 (1H, m, $W_{1/2}$=20 Hz, 3-H), 6.10 (1H, m, 9-H), 6.92 (1H, s, 6-H). MS *m/e* (rel. intensity %): 250 (M^+, 5), 235 ($[M-CH_3]^+$, 55), 217 ($[M-CH_3-H_2O]^+$, 100). IR and NMR spectral data of **27a** were in good agreement with those of (−)-petasitol reported by Naya *et al.*[12,13)] (±)-3-Epipetasitol (**28**): *Anal.* Calcd. for $C_{15}H_{22}O_3$: C, 71.97; H, 8.86; Mol. Wt. 250.1570. Found: C, 71.77; H, 8.91; M^+, 250.1541. IR cm^{-1}: 3430, 3360 (OH), 1660 (CO), 1610 (C=C). UV λ_{max}^{EtOH} 248 nm (ε 11700). NMR δ: 1.28 (3H, d, J=7 Hz, 4-CH_3), 1.37 (3H, s, 5-CH_3), 1.47 (6H, s, $-\!\!<\!\begin{smallmatrix}CH_3\\OH\\CH_3\end{smallmatrix}$), 3.90 (1H, m, $W_{1/2}$=6 Hz, 3-H), 6.12 (1H, m, 9-H), 6.93 (1H, s, 6-H). MS *m/e* (rel. intensity %): 250 (M^+, 4), 235 ($[M-CH_3]^+$, 69), 217 ($[M-CH_3-H_2O]^+$, 57), 175 (100).

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