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Diterpenoids. XLI.[1] Rearrangement of Deisopropyl Phenacylidene Type Diterpene by Means of Aluminum Chloride

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The reaction of the deisopropyl phenacylidene ester (**6**) gave the rearranged deisopropyl phenacylidene ester (**7**), as a major product, in company with the γ-lactone (**8**) in the same manner as the phenacylidene ester (**2**). On the other hand, the reaction of the deisopropyl-10α-phenacylidene ester (**9**), which has steric hindrance due to 1,3-diaxial relations between 4-methoxycarbonyl group and 10-methyl group, afforded a large portion of the starting material (**9**) in company with a small amount of the rearranged deisopropyl phenacylidene ester (**10**). Next, the reaction of the enol acetate (**32**) gave only the enol compound (**33**) in the accompany of deacetylation.

In our preceding work,[3] it was ascertained that reaction of methyl 13-isopropyl-7-oxo-podocarpa-5,8,11,13-tetraen-15-oate[4] (phenacylidene ester, **2**) derived from dehydroabietic acid (**1**) with aluminum chloride gave 13-isopropyl-1α-methyl-1β-methoxycarbonyl-7-oxo-15,16-bisnor-10α-podocarpa-5,8,11,13-tetraene (**3**), as a main product (57%) in company with 10α-hydroxy-13-isopropyl-7-oxo-1,10-seco-spiro (1.5)-podocarpa-8,11,13-trien-15-oic acid 15→10 lactone (**4**), as a minor one (5%) and the starting material (**2**: 15%). This rearrangement is completely different from an interesting reversible methyl migrations (**2**⇄**5**) under acidic conditions as illustrated in Chart 1.

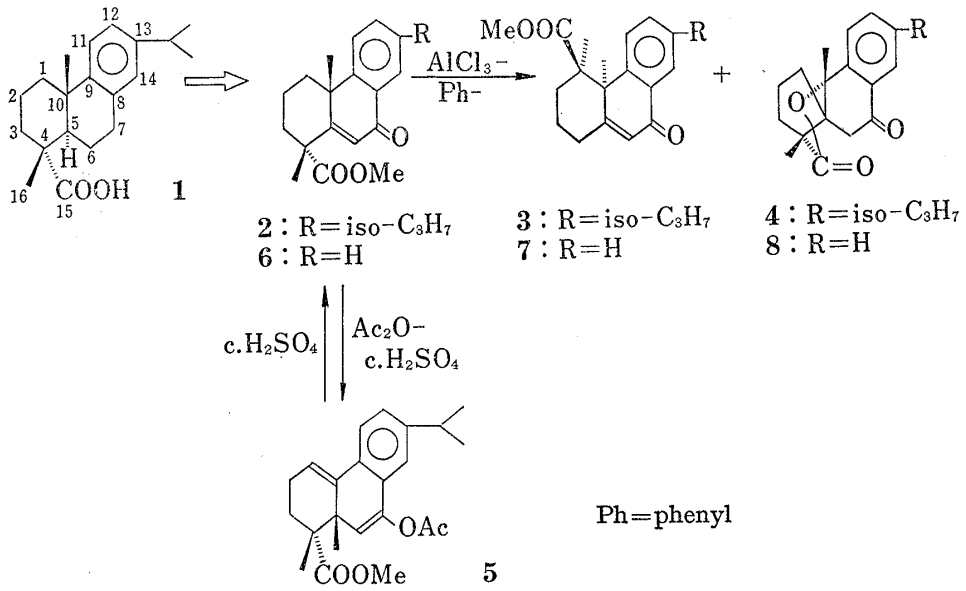


Chart 1

By extending this investigation, effect of both 13-isopropyl group in dehydroabietic acid type phenacylidene ester and steric hindrance because of 1,3-diaxial relations between

1) Part XL: T. Ohsawa, H. Mizuno, T. Takizawa, M. Itoh, S. Saito, and A. Tahara (the late), *Chem. Pharm. Bull.* (Tokyo), **24**, 705 (1976).
2) Location: *Wako-shi, Saitama-ken, 351, Japan.*
3) H. Akita and A. Tahara (the late), *Chem. Pharm. Bull.* (Tokyo), **23**, 2660 (1975).
4) E. Wenkert, R.W.J. Carney, and C. Kaneko, *J. Am. Chem. Soc.*, **83**, 4440 (1961).

4-methoxycarbonyl group and 10-methyl group in podocarpic acid type phenacylidene ester were examined in the present study.

Methyl 7-oxo-podocarpa-5,8,11,13-tetraen-15-oate[5] (deisopropyl phenacylidene ester, **6**) was stirred at reflux for 12 hours with a large excess of aluminum chloride in anhydrous benzene to give 1α-methyl-1β-methoxycarbonyl-7-oxo-15,16-bisnor-10α-podocarpa-5,8,11,13-tetraene (**7**), a brown oil (2,4-dinitrophenylhydrazone, mp 225—226°), as a main product (53%) and 10α-hydroxy-7-oxo-1,10-seco-spiro (1.5)-podocarpa-8,11,13-trien-15-oic acid 15→10 lactone (**8**), pale yellow plates, mp 212.5—213.5°, as a minor one (4%), together with the starting material (**6**: 24%) as illustrated in Chart 1. The structure of both compounds **7** and **8** was determined by the similarity of both infrared spectrum (IR) and nuclear magnetic resonance (NMR) of both the known phenacylidene ester (**3**)[3] and the known lactone (**4**)[3] except the isopropyl group as shown in Table I. It can be seen from above description that the effect of 13-isopropyl group in dehydroabietic acid type phenacylidene ester was not noticed.

Table I. Physical Constants of **3**, **4**, **7**, and **8**

	IR	NMR
3	ν_{max}^{KBr} cm^{-1} 1728, 1658	1.53, 1.62 (each s, 3H; 1-Me, 10-Me) 3.17 (s, 3H; COOMe) 6.39 (s, 1H; 6-H)
7	$\nu_{max}^{CCl_4}$ cm^{-1} 1725, 1660	1.51, 1.61 (each s, 3H; 1-Me, 10-Me) 3.14 (s, 3H; COOMe) 6.34 (s, 1H; 6-H)
4	ν_{max}^{KBr} cm^{-1} 1767, 1692	1.27 (s, 3H; 10-Me) 1.54 (s, 3H; 4-Me) 2.86 (s, 2H; 6-H_2)
8	ν_{max}^{KBr} cm^{-1} 1767, 1700	1.26 (s, 3H; 10-Me) 1.56 (s, 3H; 4-Me) 2.87 (s, 2H; 6-H_2)

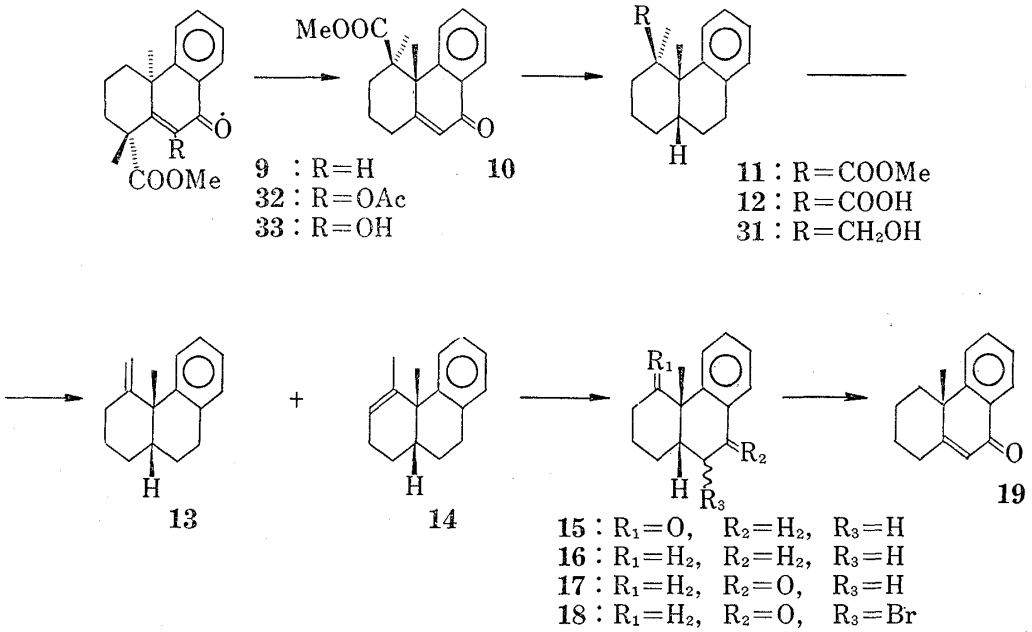


Chart 2

Under the same condition (a large excess of aluminum chloride, reflux, 12 hr) as used for **6**, methyl 7-oxo-10α-podocarpa-5,8,11,13-tetraen-15-oate (**9**)[5] was reacted to give a small amount of 1α-methyl-1β-methoxycarbonyl-7-oxo-15,16-bisnor-podocarpa-5,8,11,13-tetraene (**10**: 16%), colorless prisms, mp 113—113.5° and the starting material (**9**: 77%) as illustrated in Chart 2. The structure elucidation of the product (**10**) was successfully achieved by the

5) M. Ohta and L. Ohmori, *Chem. Pharm. Bull.* (Tokyo), **5**, 96 (1957).

chemical transformations as well as spectral examinations. At first, in order to clarify the mother skeleton, the following sequence of degradative transformations of **10** were carried out (Chart 2). Catalytic hydrogenation and hydrogenolysis of **10** over palladium-charcoal gave deisopropyl ester (**11**), which was converted to the free carboxylic acid (**12**) by alkaline hydrolysis. The stereochemistry of **11** will be later discussed in detail. The acid (**12**) was then oxidatively decarboxylated with lead tetraacetate[6] to give a mixture of exo-(**13**) and endo-olefinic compounds (**14**) in the ratio 2.7 : 1 by gas–liquid chromatography (GLC) analysis. The mixture was ozonolyzed in dichloromethane with dry ice-acetone cooling followed by treating with 30% hydrogen peroxide to afford the 1-oxo derivative (**15**) from the neutral fraction of the reaction mixture. Finally **15** was converted into the corresponding 1-de-oxo phenacylidene compound, 7-oxo-15,16-bisnor-podocarpa-5,8,11,13-tetraene (**19**), through the hydrocarbon (**16**), its 7-oxo (**17**) and 6-bromo-7-oxo derivatives (**18**) successively by the Huang-Minlon reduction of **15**, chromic anhydride oxidation of **16** in acetic anhydride, bromination of **17** and dehydrobromination of **18** with 1,5-diazabicyclo [5.4.0] undecene-5 (DBU).[7]

For the sake of direct comparison, the authentic sample was unambiguously synthesized from deisopropyl dehydroabietic acid (**20**)[8] as illustrated in Chart 3.

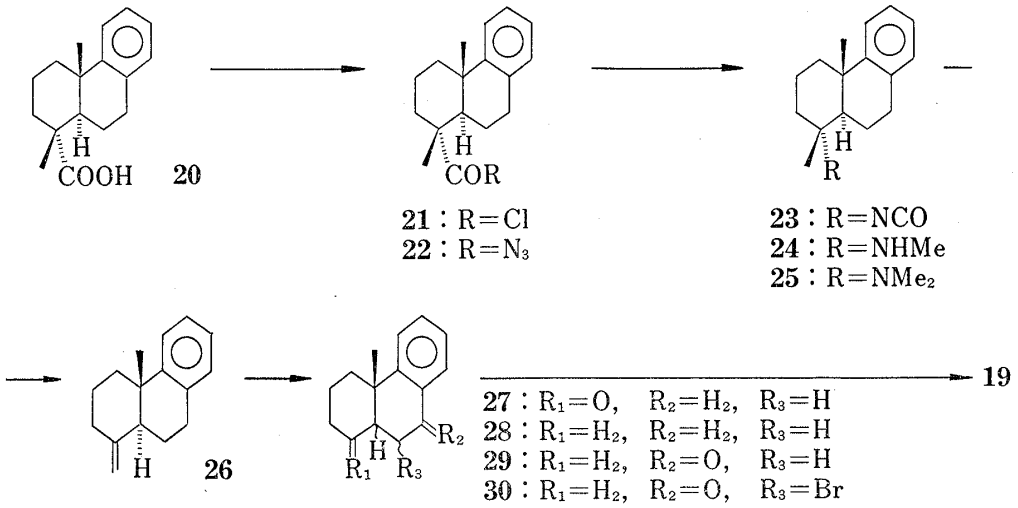


Chart 3

Deisopropyl dimethylamino compound (**25**: picrate, mp 221.5—222.5°) was derived from **20** by the analogous method to that used in dehydroabietic acid series.[9] Treatment of **25** in dichloromethane with *m*-chloroperbenzoic acid gave only exo-olefinic compound (**26**). Finally successive treatment of **26** by practically the same procedures as those used in the conversion of **13** to **19** gave the deisopropyl phenacylidene (**19**: 2,4-dinitrophenylhydrazone, mp 183—184°) *via* **27**, **28**, **29**, and **30**.

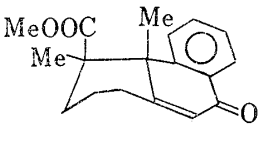
Both the deisopropyl phenacylidene compound (**19**) derived from **10** and the authentic sample (**19**) derived from **20** have completely the same physical properties (IR, NMR, Mass spectra, retention time in GLC and optical rotatory dispersion (ORD)). As 10-methyl group of **19** has β-configuration, that of **10** has β-configuration, and further, the mother skeleton of **10** is proved to be 6-6-6 membered ring system.

As for the structure of the product which is expected in the reaction of **9** with aluminum chloride, the known product (**6**) is formally conceivable in addition to **10**. Physical property

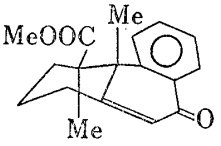
6) *a*) J.W. Huffman and P.G. Arapakos, *J. Org. Chem.*, **30**, 1604 (1965); *b*) C.R. Bennett, R.C. Cambie, R.A. Franich, and T.J. Fullerton, *Aust. J. Chem.*, **22**, 1711 (1969).
7) M. Fieser and L. Fieser, "Reagents for Organic Synthesis," Vol. 2, John Wiley and Sons, Inc., New York, 1969, p. 101.
8) M. Ohta and L. Ohmori, *Chem. Pharm. Bull.* (Tokyo), **5**, 91 (1957).
9) H.H. Zeiss and W.B. Martin, *J. Am. Chem. Soc.*, **75**, 5935 (1953).

of **6** did not agree with that of the reaction product. Thus the structure **6** was ruled out. The structure of **10** is supported by its IR (ν_{max}^{KBr} 1662 cm^{-1} for conjugated ketone and ν_{max}^{KBr} 1728 cm^{-1} for ester) and NMR spectral examination as follows. NMR analysis of **10** elucidated the proposed position and configuration of its gem-methyl-methoxycarbonyl group. A nuclear Overhauser effect (NOE) (by 100 MHz) was distinctly observed on 11-hydrogen[10] by irradiation at lower field (23.1% increase by irradiation at δ 1.80 and no observation on 11-hydrogen by irradiation at δ 0.73). These observation can be well explained from inspection of a molecular model of **10**. In the case of chair form conformation on A-ring as shown in Fig. 1, methoxycarbonyl group at 1-position comes into contact with the 11-hydrogen, and above-mentioned NOE observation is not explained clearly. On the contrary, in the case of twist boat form conformation on A-ring as shown in Fig. 1, 1-methyl group is spatially held in the plane of benzene ring and is drawn near 11-hydrogen, and is affected by anisotropic effect due to ester carbonyl group. 10-Methyl is shifted upfield by the anisotropic effect due to ester carbonyl group in comparison with usual case (*e.g.*, **7**: δ 1.51 or 1.61). Therefore it is decided that an another methyl group is located at 1-position near 11-hydrogen and chemical shift due to 1- and 10-methyl groups of **10** are δ 1.80 and δ 0.73 respectively. Inspection of both above-mentioned NMR analysis and chemical correlation indicates evidently that gem-methylmethoxycarbonyl group exists at 1-position, and methyl group has α-configuration and methoxycarbonyl group has β-configuration.

Thus the structure of **10** was unequivocally established.

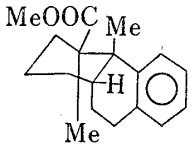


10 twist-boat form

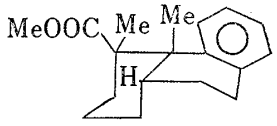


10 chair form

Fig. 1



11 A/B-*cis* (nonsteroid)



11 A/B-*cis* (steroid)

Fig. 2

TABLE II. Chemical Shift due to 1- and 10-Methyl Groups of **10**, **11**, and **31**

	10	**11**	**31**
1-Me	1.80	1.02	0.70
10-Me	0.73	1.55	1.48

Further, **11** obtained in the course of conversion of **10** into **19** was reduced with lithium aluminum hydride to the corresponding alcohol (**31**), and comparison of their NMR spectra revealed that **11** had a *cis* A/B-ring junction of a nonsteroidal conformation. The resonance signals of **11** at δ 1.02 and 1.55 can be assigned to 1-methyl and 10-methyl protons respectively, since the conversion of methoxycarbonyl group to hydroxymethyl group caused a fairly upfield of the former (to δ 0.70) but only a slight one of the latter (to δ 1.48). In addition, the fact that 10-methyl signal of **11** appears at lower field as compared with the usual case is explicable by assuming that 10-methyl group is spatially held in the plane of benzene ring and deshielded by its anisotropic effect. Inspection of a molecular model indicates evidently that a *cis* A/B-junction of a nonsteroidal conformation is the correct configuration of **11** in full agreement with the above observations (Fig. 2).

The reaction of podocarpic acid type phenacylidene ester is less than the reaction of dehydroabietic acid type phenacylidene ester with respect to the yield. In order to improve the yield of the rearranged product (**10**), the effect both other Lewis acid (or acid) and solvent was examined. Every cases, boron trifluoride etherate and dry hydrogen chloride gas in place

10) The signal due to 11-hydrogen was clearly appeared by 100 MHz NMR analysis.

of aluminum chloride as an acid, toluene, xylene, and nitrobenzene instead of benzene as a solvent, gave the starting material (**9**) or inseparable mixture.

On the other hand, under the same condition (a large excess of aluminum chloride, reflux, 12 hr) as used for **6**, methyl 6-acetoxy-7-oxo-10α-podocarpa-5,8,11,13-tetraen-15-oate (**32**)[11] was reacted to give quantitatively methyl 6-hydroxy-7-oxo-10α-podocarpa-5,8,11,13-tetraen-15-oate (**33**)[11] in the accompany of deacetylation.

In conclusion, in the reaction of the deisopropyl phenacylidene ester (**6, 9**) with aluminum chloride, the reaction is occurred in the same manner as the phenacylidene ester (**2**) with the exception of the yield. Podocarpic acid type phenacylidene ester (**9**) is less reactive than dehydroabietic acid type phenacylidene ester (**2, 6**), because it can be considered that steric hindrance due to 1,3-diaxial relations between 4-methoxycarbonyl group and 10-methyl group in the former is attributable to the drop of the yield.

Experimental[12]

Rearrangement of Methyl 7-Oxo-podocarpa-5,8,11,13-tetraen-15-oate (6) to 1α-Methyl-1β-methoxycarbonyl-7-oxo-15,16-bisnor-10α-podocarpa-5,8,11,13-tetraene (7) and 10α-Hydroxy-7-oxo-1,10-seco-spiro (1.5)-podocarpa-8,11,13-trien-15-oic Acid 15➡10 Lactone (8)——A mixture of **6**[5] (3.104 g) and $AlCl_3$ (31 g) in dry benzene (60 ml) was refluxed for 12 hr with stirring, poured into ice-water and extracted with ether. The extract was washed with sat. Na_2CO_3 aq., sat. NaCl aq., and dried over Na_2SO_4. Removal of the solvent gave a brown oil (3.309 g), which was chromatographed on silicagel (100 g) to be separated into three fractions. The first fraction (753 mg; 24% yield) eluted with petr. ether–ether (4: 1) was identified as the starting material (**6**) by GLC. The second one (1.655 g; 53% yield) subsequently obtained was the homogeneous oil (**7**). A part of **7** was treated with 2,4-dinitrophenylhydrazine to give the 2,4-dinitrophenylhydrazone, which was recrystallized from AcOEt–EtOH to give the red needles, mp 225—226°. *Anal.* Calcd. for $C_{24}H_{24}O_6N_4$: C, 62.06; H, 5.21; N, 12.06. Found: C, 61.90; H, 5.24; N, 12.26. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1725, 1660. NMR δ: 1.51, 1.61 (each s, 3H; 1-, 10-Me), 3.14 (s, 3H; COOMe), 6.34 (s, 1H; 6-H), 7.16—7.69 (m, 3H; 11-, 12-, 13-H), 8.10—8.26 (m, 1H; 14-H). The third fraction (120 mg; 4% yield) eluted with ether was recrystallized from MeOH to give **8** (116 mg), pale yellow plates, mp 212.5—213.5°. *Anal.* Calcd. for $C_{17}H_{18}O_3$: C, 75.53; H, 6.71. Found: C, 75.47; H, 6.75. IR ν_{max}^{KBr} cm^{-1}: 1767, 1700. NMR δ: 1.26 (s, 3H; 10-Me), 1.56 (s, 3H; 4-Me), 2.87 (s, 2H; 6-H_2) 7.20—7.60 (m, 3H; 11-, 12-, 13-H), 7.97—8.13 (m, 1H; 14-H).

Rearrangement of Methyl 7-Oxo-10α-podocarpa-5,8,11,13-tetraen-15-oate (9) to 1α-Methyl-1β-methoxycarbonyl-7-oxo-15,16-bisnor-podocarpa-5,8,11,13-tetraene (10)——A mixture of **9**[5] (4 g) and $AlCl_3$ (40 g) in dry benzene (80 ml) was refluxed for 12 hr with stirring. The reaction mixture was treated as described above for **6** to give brown oil (4.965 g), which was chromatographed on silica gel (100 g) to be separated into two fractions. The first fraction (3.061 g; 77% yield) eluted with petr. ether–ether (4: 1) was recrystallized from petr. ether–ether to give **9** (2.993 g), colorless prisms and identified as the starting material by GLC. The second one (645 mg; 16% yield) subsequently obtained was recrystallized from petr. ether–ether to give **10** (595 mg), colorless prisms, mp 113—113.5°. *Anal.* Calcd. for $C_{18}H_{20}O_3$: C, 76.03; H, 7.09. Found: C, 75.76; H, 7.11. IR ν_{max}^{KBr} cm^{-1}: 1728, 1662. NMR δ: 0.73 (s, 3H; 10-Me), 1.80 (s, 3H; 1-Me), 3.78 (s, 3H; COOMe), 6.49 (s, 1H; 6-H), 7.10—7.68 (m, 3H; 11-, 12-, 13-H), 8.20—8.36 (m, 1H; 14-H). NOE (100 MHz): Irradiation at δ 1.80 increased the area of peak due to 11-H by 23.1%.

Hydrogenation and Hydrogenolysis of 10 to 1α-Methyl-1β-methoxycarbonyl-15,16-bisnor-5β-podocarpa-8,11,13-triene (11)——A solution of **10** (415 mg) in AcOH (20 ml)–conc. H_2SO_4 (1 drop) was hydrogenated at ordinary temperature and pressure over 10% Pd-C (200 mg). After hydrogen absorption had ceased, the catalyst was filtered off and the filtrate was evaporated under reduced pressure. The ether extract of the resulting residue was washed with sat. Na_2CO_3 aq., sat. NaCl aq., and then dried over Na_2SO_4. Removal of the solvent gave crystals (380 mg), which were recrystallized from MeOH to give **11** (317 mg), colorless prisms, mp 118.5—119.5°. *Anal.* Calcd. for $C_{18}H_{24}O_2$: C, 79.37; H, 8.88. Found: C, 79.08; H, 8.69. IR ν_{max}^{KBr} cm^{-1}: 1707. NMR δ: 1.02 (s, 3H; 1-Me), 1.55 (s, 3H; 10-Me), 3.67 (s, 3H; COOMe), 7.10 (br. s, 4H; aromatic H).

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11) *a*) A. Tahara, O. Hoshino, and Y. Hamazaki, *Chem. Pharm. Bull.* (Tokyo), **11**, 1328 (1963); *b*) *Idem*, *Sci. Papers Inst. Phys. Chem. Res.*, **58**, 15 (1964).

12) All melting points were measured on the Kofler block and were uncorrected. NMR spectra were measured (δ) at 60 MHz in $CDCl_3$ *vs.* Me_4Si as internal reference. High-resolution mass spectra were taken with JMS-01SG spectrometer. GLC was measured under the column condition (2 m×4 mm, 1.5% OV-17 on Shimalite W (80—100 mesh)).

Hydrolysis of 11 to 1β-Carboxy-1α-methyl-15,16-bisnor-5β-podocarpa-8,11,13-triene (12)——A solution of **11** (840 mg) and KOH (2 g) in diethylene glycol (20 ml) was heated at 150° for 12 hr with stirring, and the reaction mixture was diluted with H_2O and extracted with ether (neutral fraction). The aqueous solution was acidified with 10% HCl and extracted with ether (acidic fraction). Both ether extracts were separately washed with sat. NaCl aq., dried over Na_2SO_4 and evaporated. The former gave an oil (121 mg) and the latter gave 707 mg of **12** as crystals. The corresponding methyl ester (**11**) was identified as starting (**11**). Compound (**12**) was used without further purification.

Preparation of 1-Oxo-15,16-bisnor-5β-podocarpa-8,11,13-triene (15) from 12——1) A solution of the crude **12** (1.978 g) and $Pb(OAc)_4$ (3.9 g) in dry benzene (80 ml)–pyridine (1 ml) was refluxed for 4 hr under N_2-stream. The cooled mixture was filtered and the filtrate was washed with 10% KOH aq., sat. NaCl aq., and then dried over Na_2SO_4. Removal of the solvent gave an oil (1.6 g) which was chromatographed on basic alumina (70 g) with petr. ether (600 ml) to give a mixture (1.007 g), gas chromatography of which indicated the presence of 1-methylene-15,16-bisnor-5β-podocarpa-8,11,13-triene (**13**) and 1-methyl-15,16-bisnor-5β-podocarpa-1,8,11,13-tetraene (**14**) in the ratio 2.7: 1.

2) Ozone was passed through a solution of the oily mixture of **13** and **14** (840 mg) in CH_2Cl_2 (25 ml) with dry ice-acetone cooling for 15 min, and then 30% H_2O_2 aq. (10 ml) was added at room temperature. The mixture was stirred for 1 hr, and washed with 10% KOH aq., sat. NaCl aq., and then dried over Na_2SO_4. The CH_2Cl_2 solution was evaporated to give **15** (897 mg), an oil, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1703. **15** was used without further purification.

Preparation of 7-Oxo-15,16-bisnor-podocarpa-5,8,11,13-tetraene (19) from 15——1) A solution of the crude **15** (897 mg), $NH_2NH_2 \cdot H_2O$ (2 ml) and KOH (2 g) in diethylene glycol (15 ml) was stirred and heated at 160—170° for 1 hr, and then excess hydrazine was distilled off. Another KOH (2 g) was added to the reactants which were heated at 220° for 2 hr, cooled, diluted with H_2O and extracted with ether. The extract was washed with sat. NaCl aq. and then dried over Na_2SO_4. Removal of the solvent gave 405 mg of 15,16-bisnor-5β-podocarpa-8,11,13-triene (**16**) as an oil.

2) The crude **16** was treated with CrO_3 (610 mg)–Ac_2O (10 ml) at room temperature for 12 hr with stirring. After MeOH (5 ml) was added, the reaction mixture was evaporated under reduced pressure. The residue was diluted H_2O and extracted with ether. The extract was washed with sat. Na_2CO_3 aq., sat. NaCl aq., and then dried over Na_2SO_4. Removal of the solvent gave 385 mg of 7-oxo-15,16-bisnor-5β-podocarpa-8,11,13-triene (**17**) as an oil. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1682.

3) A mixture of the crude **17** in AcOH (2 ml), 50% Br_2–AcOH (600 mg) and 13% (v/v) HBr–AcOH solution (2 drops) was stirred at room temperature for 2 hr. After red color disappeared, the reaction mixture was diluted with H_2O and extracted with ether. The extract was washed with 5% Na_2CO_3 aq., sat. NaCl aq., and then dried over Na_2SO_4. Removal of the solvent gave 449 mg of 6ξ-bromo-7-oxo-15,16-bisnor-5β-podocarpa-8,11,13-triene (**18**) as brown oil.

4) The crude **18** was heated at 100° with 1,5-diazabicyclo[5.4.0]undecene-5 (DBU) (5 ml) for 1 hr. After $CHCl_3$ was added to the cooled reaction mixture, $CHCl_3$ layer was separated, washed with 10% HCl aq., sat. NaCl aq., and then dried over Na_2SO_4. Removal of the solvent gave brown oil, which was chromatographed on silica gel (30 g) in petr. ether–ether (9: 1) to give 88 mg of **19** as a homogeneous oil. *Anal.* High-resolution mass spectrum. Calcd. for $C_{15}H_{16}O$ (M^+; *m/e*): 212.1201. Found: 212.1224. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1660. NMR δ: 1.46 (s, 3H; 10-Me), 6.25 (s, 1H; 6-H), 7.12—7.54 (m, 3H; 11-, 12-, 13-H), 8.06—8.22 (m, 1H; 14-H). ORD (*c*=0.1, EtOH) $[\phi]^{25}$ (mμ): +530 (300), 0 (306), −53 (308), 0 (310), +1245.5 (352), +901 (370), +503.5 (400), +185.5 (500). Compound (**19**) was identified as the authentic sample (**19**) as described later.

Preparation of 4-Dimethylamino-15-nor-podocarpa-8,11,13-triene (25) from Deisopropyl Dehydroabietic Acid (20)——1) **20**[8] (10.6 g) was dissolved in dry benzene (50 ml) to which $SOCl_2$ (12 ml) and pyridine (1 ml) were added. After the solution was refluxed for 2 hr with stirring, the reaction mixture was evaporated under reduced pressure. Resulting residue was diluted with H_2O and extracted with ether. The extract was washed with 1% NaOH aq., sat. NaCl aq., and then dried over Na_2SO_4. Removal of the solvent gave 10.1 g of **21** as an oil.

2) The crude **21** in acetone (250 ml) was stirred with 10% (w/v) NaN_3 aqueous solution (50 ml) for 30 min at room temperature. After the reaction mixture was concentrated under reduced pressure until one-third volume, excess H_2O was added and the resulting solution was extracted with ether. The extract was washed with sat. NaCl aq. and then dried over Na_2SO_4. Removal of the solvent gave an oil (**22**).

3) A solution of **22** in xylene (100 ml) was refluxed for 2 hr with stirring and evaporated under reduced pressure to give an oil (**23**).

4) A mixture of the cooled **23** and $LiAlH_4$ (4 g) in dry ether (200 ml) was refluxed for 2.5 hr with stirring and kept to stand for 12 hr at room temperature. The reaction mixture was diluted with H_2O and extracted with ether. After the ether layer was acidified with 10% HCl aq., the aqueous layer was alkalified with NaOH and extracted with ether again. The extract was washed with sat. NaCl aq., and then dried over Na_2SO_4. Removal of the solvent gave 6.701 g of 4-monomethylamino-15-nor-podocarpa-8,11,13-triene (**24**) as an oil.

5) After a solution of **24** in dry ether (25 ml)–CH_3I (25 ml) was kept to stand for 12 hr in a refrigerator, it was alkalified with 10% KOH aq., and extracted with ether. The extract was washed with sat. NaCl aq.,

and then dried over Na_2SO_4. Removal of the solvent gave 5.201 g of **25** as a homogeneous oil. A part of **25** was treated with picric acid to give the picrate, which was recrystallized from MeOH to give yellow prisms, mp 221.5—222.5°. *Anal.* Calcd. for $C_{24}H_{30}O_7N_4$: C, 59.25; H, 6.22; N, 11.52. Found: C, 59.24; H, 6.16; N, 11.49. NMR δ: 1.11, 1.20 (each s, 3H; 4-, 10-Me), 2.20 (s, 6H; NMe_2), 6.96—7.36 (m, 4H; aromatic H).

Degradation of 25 to 4-Methylene-15,16-bisnor-podocarpa-8,11,13-triene (26)——To a solution of **25** (4.859 g) in CH_2Cl_2 (30 ml) was added *m*-chloroperbenzoic acid (4 g) with ice-water cooling. After the solution was kept to stand for 12 hr in a refrigerator, it was washed with 10% HCl aq., 10% KOH aq., sat. NaCl aq., and then dried over Na_2SO_4. Removal of the solvent gave an oil (4.415 g), which was chromatographed on basic alumina (120 g) in petr. ether–ether (1.5 l) to give 2.613 g of **26** as a colorless oil. NMR δ: 1.00 (s, 3H; 10-Me), 4.60, 4.85 (each br. s, 1H; $>C=CH_2$), 6.98—7.38 (m, 4H; aromatic H).

Preparation of the Authentic Sample (19) from 26——1) Ozone was passed through a solution of **26** (2.613 g) in AcOEt (25 ml) with dry ice-acetone cooling for 1.5 hr and then 30% H_2O_2 aq. (20 ml) was added at room temperature. After the reaction mixture was stirred for 30 min, it was treated as described above to give 2.877 g of 4-oxo-15,16-bisnor-5ξ-podocarpa-8,11,13-triene (**27**) as an oil.

2) A solution of the crude **27**, $NH_2NH_2 \cdot H_2O$ (8 ml) and KOH (8 g) in diethylene glycol (60 ml) was stirred and heated at 160—170° for 1 hr, and then excess hydrazine was distilled off. Another KOH (8 g) was added to the reactants which were heated at 220° for 2 hr. The cooled mixture was treated as described above to give 1.195 g of 15,16-bisnor-5ξ-podocarpa-8,11,13-triene (**28**) as an oil.

3) The crude **28** was treated with CrO_3 (900 mg)–Ac_2O (32 ml) at room temperature for 12 hr with stirring. After MeOH (5 ml) was added, the reaction mixture was treated as described above to give 1.141 g of 7-oxo-15,16-bisnor-5ξ-podocarpa-8,11,13-triene (**29**) as an oil. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1682.

4) A mixture of the crude **29** in AcOH (5 ml), 50% Br_2–AcOH (1.7 g) and 13% (v/v) HBr–AcOH solution (2 drops) was stirred at room temperature for 2 hr. After red color disappeared, the reaction mixture was treated as described above to give 1.486g of 6ξ-bromo-7-oxo-15,16-bisnor-5ξ-podocarpa-8,11,13-triene (**30**).

5) The crude **30** was heated at 100° with DBU (10 ml) for 1 hr. After $CHCl_3$ was added to the cooled reaction mixture, $CHCl_3$ layer was treated as described above to give brown oil, which was chromatographed on silica gel (30 g) in petr. ether–ether (9: 1) to give 452 mg of **19** as a homogeneous oil. A part of **19** was treated with 2,4-dinitrophenylhydrazine to give the 2,4-dinitrophenylhydrazone, which was recrystallized from AcOEt–EtOH to give the red prisms, mp 183—184°. *Anal.* Calcd. for $C_{21}H_{20}O_4N_4$: C, 64.27; H, 5.14; N, 14.28. Found: C, 64.26; H, 5.17; N, 14.40. *Anal.* High-resolution mass spectrum. Calcd. for $C_{15}H_{16}O$ (M^+; *m/e*): 212.1201. Found: 212.1222.

Reduction of 11 to 1β-Hydroxymethyl-1α-methyl-15,16-bisnor-5β-podocarpa-8,11,13-triene (31)——A mixture of **11** (123 mg) and $LiAlH_4$ (100 mg) in dry ether (10 ml) was refluxed for 1 hr with stirring. The reaction mixture was diluted with H_2O, then acidified and extracted with ether. The extract was washed with sat. Na_2CO_3 aq., sat. NaCl aq., and then dried over Na_2SO_4. Removal of the solvent gave 111 mg of **31** as a homogeneous oil. *Anal.* High-resolution mass spectrum. Calcd. for $C_{17}H_{24}O$ (M^+; *m/e*): 244.1827. Found: 244.1857. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3665. NMR δ: 0.70 (s, 3H; 1-Me), 1.48 (s, 3H; 10-Me), 3.68 (s, 2H; 1-$C\underline{H}_2$-OH), 7.02—7.54 (m, 4H; aromatic H).

Reaction of Methyl 6-Acetoxy-7-oxo-10α-podocarpa-5,8,11,13-tetraen-15-oate (32) to Methyl 6-Hydroxy-7-oxo-10α-podocarpa-5,8,11,13-tetraen-15-oate (33)——A mixture of **32**[11] (1 g) and $AlCl_3$ (20 g) in dry benzene (20 ml) was refluxed for 12 hr with stirring. The reaction mixture was poured into ice-water and extracted with ether. The extract was washed with 5% Na_2CO_3 aq., sat. NaCl aq., and then dried over Na_2SO_4. Removal of the solvent gave brown oil (1.017 g), which was chromatographed on silica gel (40 g) in petr. ether–ether (4: 1) to isolate quantitatively a homogeneous oil (**33**). It was identified as the authentic compound (**33**)[11] by IR and NMR.