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# Conversion of Dehydroabietic Acid into a Steroid Skeleton: Formation of the A-Ring. I[1]

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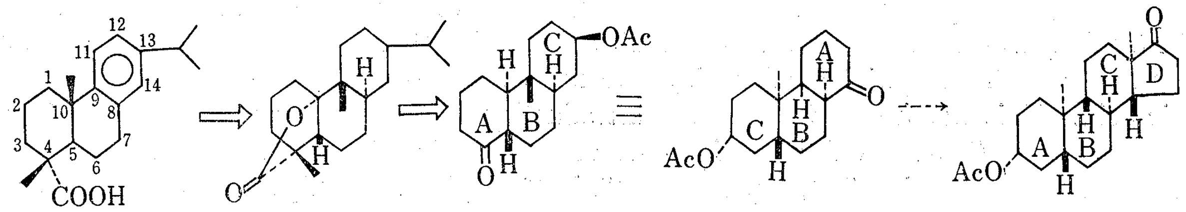
Conversion of dehydroabietic acid (**1**) to a steroid skeleton was attempted. Synthesis of the 3-oxo compound (**25**) having a steroid-type A ring was successfully completed from starting material (**9**) *via* the intermediates (**18**) and (**19**).

We have been deriving dehydroabietic acid (**1**), a representative resin acid of pine tree, into physiologically active compounds as part of studies for the development and utilization of pine resin. Attempts have been made for the conversion of **1** to a steroid skeleton and a few of our results have been published. The first was a project for the synthesis of a steroid antipode and synthesis of an oxo compound (**3**), regarded as its important intermediate, has been reported[3] (Chart 1). This synthesis started with the lactone (**2**) with 9-methyl transited from 10-position, and this was converted to the oxo compound (**3**) in which the A, B and C rings in dehydroabietic acid (**1**) corresponded to the C, B and A rings of the steroid skeleton (**4**).



1 2 3 4

Chart 1

In order to form the D ring in a steroid, a five-membered ring was formed by the use of the side chain in **5** and **6** derived from **1**, and compounds (**7** and **8**) possessing a steroid skeleton were obtained[4] (Chart 2).

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1) This paper constitutes Part XXXII of "Diterpenoids" series by A. Tahara and co-workers. Part XXXI: A. Tahara and H. Akita, *Chem. Pharm. Bull.* (Tokyo), 23, 1984 (1975).
Melting points were determined on a micro hot-stage and were uncorrected. Infrared (IR) spectra ($\nu_{max}$ cm$^{-1}$) were recorded on a JASCO IR-G. Nuclear magnetic resonance (NMR) spectra ($\delta$) were measured at 60 MHz in $CCl_4$ unless otherwise specified (5—10% solution *vs.* tetramethylsilane as internal reference) with a Varian T-60. Mass spectra were taken on a JEOL JMS-OlS. Circular dichroism (CD) curve was measured in MeOH with a JASCO J-20. Every thin-layer chromartography (TLC) was carried out on Silica gel G plates and shown by *Rf* values and preparative TLC (pre TLC) was carried out with Silica gel G–Silica gel $PF_{254}$ (2: 1) as adsorbent. Gas–liquid chromatography (GLC) (1.5% OV-17 on Shimalite W (80—100 mesh), 2 m×4 mm) was shown by $t_R$ values.

2) Location: *a) Wako-shi, Saitama, 351, Japan*; *b) Minato-ku, Tokyo, 108, Japan.* To whom inquiries regarding this report should be addressed.

3) A. Tahara, Y. Harigaya, and M. Onda, *Chem. Pharm. Bull.* (Tokyo), **20**, 459 (1972).

4) A. Tahara, M. Shimagaki, M. Itoh, Y. Harigaya, and M. Onda, *Chem. Letters*, (Japan), **1974**, 651.

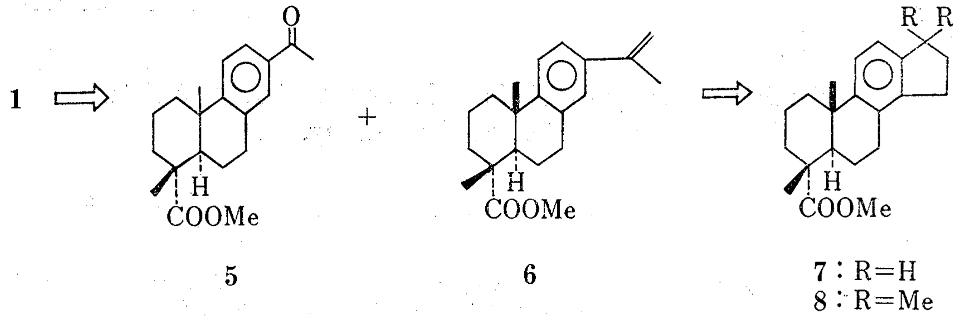

Chart 2

Studies on the conversion of abietic acid to steroidal skeleton have been carried out in other countries,[5] and synthesis of a steroid skeleton (antipode) has recently been reported by Jeger and others.[6]

In the present series of work, we took up the next problem in the conversion of pine resin to the steroids, *i.e.*, formation of the A ring, and succeeded in the synthesis of the 3-oxo compound (**25**) possessing the A ring of a steroid, *via* the intermediates (**18**) and (**19**), which is described herein.

The benzonilidene compound (**9**),[7] easily obtained from dehydroabietic acid (**1**), was submitted to enol acetylation with acetic anhydride-*p*-toluenesulfonic acid or isopropenyl acetate-*p*-toluenesulfonic acid for introduction of 4—5 double bond, but a stable and single substance was not obtained. Since it had been found in our laboratory[8] that compounds possessing a benzonilidene system underwent various rearrangement under acidic condition, **9** must have given a complex products. In order to introduce a double bond into the 3—4 position of **9**, the objective $\Delta^3$-benzonilidene compound (**10**) was obtained as an oil in *ca.* 70% yield by dehydrogenation of **9** with chloranil–acetic acid, though the starting material was recovered when treated with dichlorodicyanobenzoquinone–benzene or with selenium oxide–acetic acid. This was a step towards the introduction of a substituent into the 3-position. $\Delta^3$-Benzonilidene (**10**) was oxidized with *m*-chloroperbenzoic acid– or monoperphthalic acid–chloroform to the epoxide (**11**), mp 110—111°, in 85% yield. Configuration of the epoxide ring has not been confirmed directly but was considered to be $\alpha$ from the assumptions made later.

Cleavage of **11** with boron trifluoride etherate to introduce an oxo group into 3-position resulted in a labile product which could not be examined in detail. In an attempt to effect reductive cleavage of the epoxide ring in **11** with concurrent reduction of the 5—6 double bond, catalytic reduction of **11** with 10% palladium-carbon in ethyl acetate–conc. sulfuric acid was carried out. But, before reductive cleavage of the epoxide ring, it was hydrolyzed into the diol and only the 5—6 double bond was reduced, forming **13**, mp 198°. Configuration of the 5-position was determined to be $5\beta$-H (*cis*-A/B ring) by identification with the sample of **13** obtained by another route. The epoxide ring in **11** was therefore cleaved by treatment with perchloric acid–acetone to obtain the diol (**12**), mp 192—193.5°. Since the chemical shift of 10-methyl in the NMR spectrum of **12** shifts 0.4 ppm to the lower magnetic field from

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[5] H.H. Zeiss and W.B. Martin, *J. Am. Chem. Soc.*, **75**, 5935 (1953); B.R. Davis and W.B. Watkins, *Tetrahedron*, **24**, 2165 (1968); J.W. Huffman, *J. Org. Chem.*, **35**, 478 (1970) and references cited therein; R.C. Cambie and R.A. Franich, *Aust. J. Chem.*, **24**, 117 (1971) and references cited therein.

[6] T. Wirthlin, H. Wehrli, and O. Jeger, *Helv. Chem. Acta*, **57**, 351, 368 (1974).

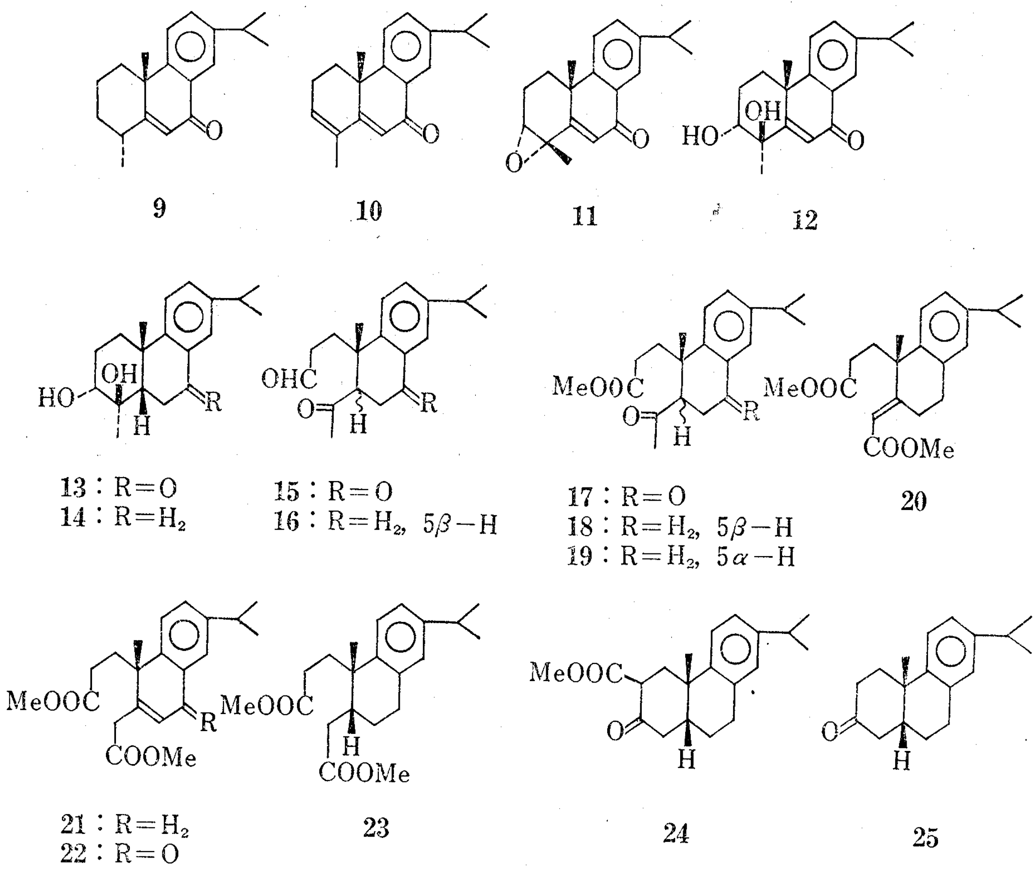
[7] E. Wenkert, R.W.J. Carney, and C. Kaneko, *J. Am. Chem. Soc.*, **83**, 4440 (1961) and references cited therin.

[8] A. Tahara, H. Mizuno, and T. Ohsawa, *Chem. Letters* (Japan), **1972**, 1163; A. Tahara, H. Akita, T. Takizawa, and H. Mizuno, *Tetrahedron Letters*, **1974**, 2837.

$\delta$ 1.30 in **11**, 4-OH and 10-Me are in 1,3-diaxial state,[9] so that the configuration of the two hydroxyls in **11** are 3α-OH and 4β-OH. From the fact that the half-width value ($W_{h/2}$) of 3-H is 8 Hz, 3-OH would be axial. In many of the steroids, cleavage of the α,β-unsaturated epoxide by an acid occurs of the allylic position.[10] Considering these facts, it seems possible to assume that the epoxide ring in **11** underwent cleavage at 4-position to form the 3α, 4β-diol (**12**) and the α-configuration of the epoxide ring in **11** seems appropriate.

Catalytic reduction of **12** over platinum oxide–acetic acid to eliminate the benzonilidene system resulted in the reduction of 5—6 double bond, giving the diol (**13**), mp 197—197.5°. The chemical shift of 4α-Me appeared in a higher field ($\delta$ 0.53) in the NMR spectrum of **13**. This was taken to mean that 4α-Me was situated spatially above the benzene ring and was affected by its anisotropy. Therefore the A/B ring juncture must be *cis* (5β-H).

Oxidative cleavage of **13** with lead tetraacetate and methylation of the acid product with diazomethane gave an oxo ester (**17**). Oxidative cleavage of **13** with periodic acid–dioxane gave only an aldehyde (**15**), whose further oxidation with potassium permanganate and methylation of the acid product (*ca.* 10—30% yield) gave a product agreeing with the oxo ester (**17**) obtained as above. Thus, oxidative cleavage of **13** resulted in irregular or poor yield of the product and, in order to improve this point, cleavage was attempted after removal of the 7-oxo group.



9 10 11 12

13 : R=O
14 : R=$H_2$

15 : R=O
16 : R=$H_2$, 5β−H

17 : R=O
18 : R=$H_2$, 5β−H
19 : R=$H_2$, 5α−H

20

21 : R=$H_2$
22 : R=O

23 24 25

Chart 3

As stated earlier, 7-oxo group was not reduced by catalytic reduction of **12**, and reduction of **13** was attempted in another way. The Clemmensen reduction of **13** did give the desired

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9) N.S. Bhacca and D.H. Williams, "Applications of NMR Spectroscopy in Organic Chemistry," Holden-Day Inc., San Francisco, 1964, p. 13.

10) C. Djerassi, "Steroid Reaction," Holden-Day Inc., San Francisco, 1962, p. 615.

product (**14**) and another by-product in 1:1 ratio, while reduction with aluminum chloride–lithium aluminum hydride lowered the proportion of the by-product to 10%, as detected by GLC and NMR spectral analysis. This product (**14**) containing 10% of a by-product was submitted to cleavage with periodic acid and the resulting aldehyde (**16**) (IR: 2700) was oxidized with potassium permanganate, followed by methylation of the product with diazomethane, finally affording the 5β-oxo ester (**18**), mp 82°, in 20% yield from **14**. Hydrolysis of **18** with 10% potassium hydroxide–methanol, followed by methylation with diazomethane resulted in isomerization of the 5-position to give the 5α-oxo ester (**19**). Compounds (**18** and **19**) can be regarded as the important intermediates for the synthesis of the objective 3-oxo compound (**25**). The structure of **19** was confirmed by later synthesis using a compound with reliable configuration of the 5-position, which will be described in a subsequent paper.[11]

The two oxo esters (**18** and **19**) were brominated with bromine in acetic acid–hydrobromic acid mixture, submitted to the Favorskii rearrangement with 3% potassium hydroxide–methanol, and methylation of the resulting product with diazomethane afforded the corresponding diesters (**20** and **21**), position isomers of the double bond. The double bond in **20** slowly underwent isomerization to change into **21** when left in the air or under alkaline condition (3% potassium hydroxide–methanol) as detected by TLC. When left in the air, **21** rapidly changed into another compound (**22**) with formation of a new α,β-unsaturated ketone as detected in its IR spectrum (1660). This fact proved that the double bond is present in 4—5 position in **20** and in 5—6 position in **21**.

Catalytic reduction of a mixture of **20** and **21** over platinum oxide–acetic acid gave a 5β-diester (**23**), whose β-configuration of 5-position in **23** will be described later. Dieckmann condensation of **23** with sodium triphenylmethane afforded a six-membered ring oxo ester (**24**) which was found to be partially enolized from its IR absorptions of 1750, 1720 (oxo ester), and of 3600—2300, 1660, 1620 (enol ester). Hydrolysis of **24** with 10% potassium hydroxide–methanol gave the 3-oxo compound (**25**) in 15% yield from **23**.

As shown in Fig. 1, the CD spectrum of the 3-oxo group in **25** gives a negative curve. In order to determine the steric structure of the A/B ring juncture in **23** and **25**, CD curve

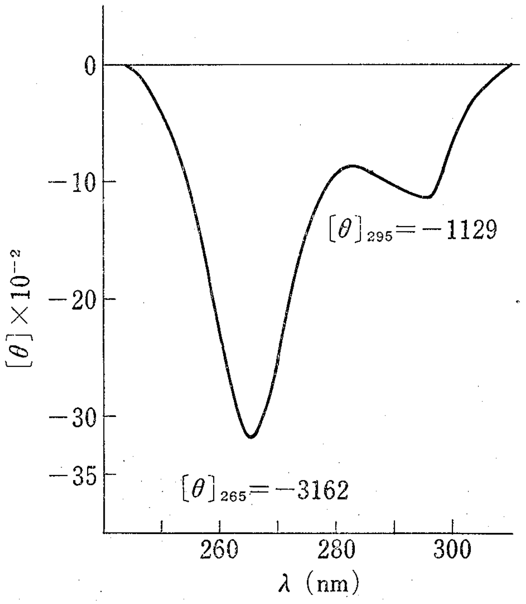

Fig. 1. Circular Dichroism Curve (MeOH soln.) of **25**

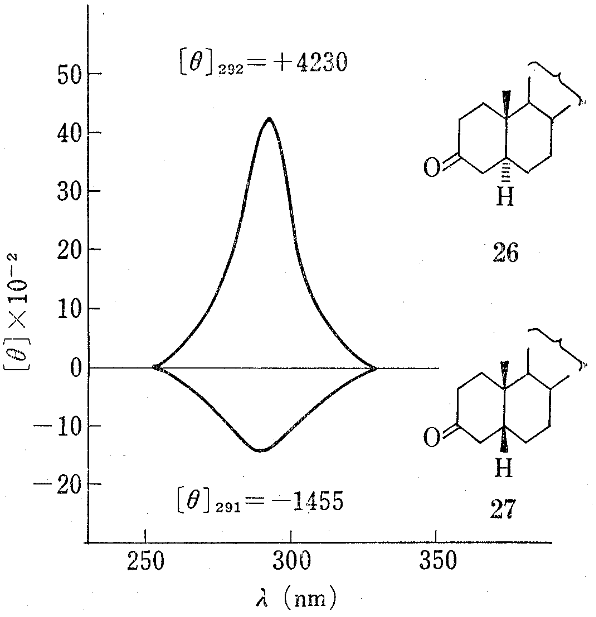

Fig. 2. Circular Dichroism Curves (MeOH soln.) of **26** and **27**

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[11] A. Tahara, Y. Harigaya, and M. Onda, *Chem. Pharm. Bull.* (Tokyo), 23, 1996 (1975).

of **25** was compared with those of the two isomers (Fig. 2)[12] of the steroid as a standard, **26** (*trans*-5α-H/10β-Me) and **27** (*cis*-5β-H/10β-Me). Thus the A/B ring juncture in **25** and **23** was determined as *cis*-5β-H/10β-Me.

As shown above, conversion of dehydroabietic acid (**1**) to the 3-oxo compound (**25**) was successful and the structure of **25** was determined. The 3-oxo compound (**25**) has the A-B-C ring structure of the steroid, and it is hoped that the synthesis of the steroid will be attempted by using **25** as the important intermediate and by combination of the five-membered ring (D ring in steroid) formation reaction using the isopropyl side chain developed previously.[4]

## Experimental

**13-Isopropyl-7-oxo-15-nor-podocarpa-3,5,8,11,13-pentaene (10)**——To a solution of dienone (9)[7] (6.6 g) and *p*-TsOH·$H_2O$ (0.3 g) in AcOH (400 ml) was added chloranil (6.0 g). After the reaction mixture was refluxed for 8 hr, the precipitates were filtered off and the solvent was evaporated under reduced pressure. The resulting residue was dissolved in hexane and the work-up in the usual way yielded a neutral yellow oil (5.2 g). A part of the oil (0.5 g) was chromatographed on silica gel (40 g) to give light yellow oil (10) (0.45 g) from hexane:benzene (1:4—1:5) eluate. Mass Spectrum: Calcd. for $C_{19}H_{22}O$ ($M^+$, *m/e*): 266.1671. Found: 266.1682. $t_R=11.5$ (205°). IR ($CCl_4$): 1650, 1640. NMR: 1.31 (6H, d, $J=7$ Hz; $CHMe_2$), 1.38 (3H, s; 10-Me), 2.00 (3H, bs, $W_{h/2}=4.5$ Hz; 4-Me), 6.00 (1H, b, $W_{h/2}=9$ Hz; 3-H), 6.31 (1H, s; 6-H), 7.40 (2H, dd; 11- and 12-H), 7.97 (1H, bs, $W_{h/2}=3$ Hz, 14-H).

**3α,4α-Epoxy-13-isopropyl-7-oxo-15-nor-podocarpa-5,8,11,13-tetraene (11)**——To a solution of trienone (10) (300 mg) in $CHCl_3$ (6 ml) was added a solution of *m*-$ClC_6H_4CO_3H$ (or *o*-$C_6H_4CO_2H\cdot CO_3H$) (500 mg) in ether (5 ml). The reaction mixture was allowed to stand for 3 days at room temperature and then diluted with ether. The usual work-up gave a neutral colorless oil (300 mg), which was chromatographed on silica gel (30 g). Crystals resulted from benzene:AcOEt (98:2) eluate were recrystallized from ether to give colorless prisms (11) (270 mg), mp 110—111°. *Anal.* Calcd. for $C_{19}H_{22}O_2$: C, 80.82; H, 7.85. Found: C, 80.73; H, 7.97. IR (KBr): 1655, 1630 (sh). NMR (100 MHz): 1.25 (6H, d, $J=7$ Hz; $CHMe_2$), 1.30 (3H, s; 10-Me), 1.56 (3H, s; 4-Me), 3.06 (1H, bs, $W_{h/2}=3.8$ Hz; 3-H), 6.40 (1H, s; 6-H), 7.10 (2H, dd; 11- and 12-H), 7.66 (1H, s; 14-H).

**3α,4β-Dihydroxy-13-isopropyl-7-oxo-16-nor-podocarpa-5,8,11,13-tetraene (12)**——To a solution of epoxide (11) (110 mg) in acetone (2.0 ml) was added 15% $HClO_4$ aq. (0.1 ml). The reaction mixture was allowed to stand for 24 hr at room temperature, diluted with $H_2O$, and then extracted with AcOEt. The work-up in the usual way gave the neutral colorless crystals (100 mg), which were recrystallized from benzene to give colorless needles (12), mp 194°. An oil (65 mg) resulted from the mother liquors was chromatographed on silica gel (10 g) to give colorless crystals (42 mg) in benzene:AcOEt (4:1) eluate. *Anal.* Calcd. for $C_{19}H_{24}O_3$: C, 75.97; H, 8.05. Found: C, 75.72; H, 7.99. IR (KBr): 3375, 1652 (sh), 1648. NMR ($CD_3COCD_3$): 1.24 (6H, d, $J=6.5$ Hz; $CHMe_2$), 1.58, 1.70 (each 3H, s; 4- and 10-Me), 3.76 (2H,[13] bs, $W_{h/2}=8$ Hz; 3-H and 3- or 4-OH), 4.15 (1H,[14] s; 3- or 4-OH), 6.42 (1H, s; 6-H), 7.56 (2H, dd; 11- and 12-H), 7.89 (1H, bs, $W_{h/2}=4$ Hz; 14-H).

**3α,4β-Dihydroxy-13-isopropyl-7-oxo-16-nor-5β-podocarpa-8,11,13-triene (13)**——Dienone diol (12) (2.9 g) was hydrogenated with Pt obtained from $PtO_2$ (300 mg) in AcOH (200 ml) under an atmosphere of hydrogen. The usual work-up gave the neutral colorless crystals (2.8 g). The crystals were washed with acetone (30 ml) to give colorless crystals (1.4 g), which were recrystallized from hexane–ether to give colorless prisms (13), mp 197—197.5°. *Anal.* Calcd. for $C_{19}H_{26}O_3$: C, 75.46; H, 8.67. Found: C, 75.16; H, 8.63. IR ($CHCl_3$): 3580, 3480, 1670. NMR ($CDCl_3$): 0.53 (3H, s; 4-Me), 1.26 (6H, d, $J=7$ Hz; $CHMe_2$), 1.33 (3H, s; 10-Me), 2.83 (2H,[14] bs, $W_{h/2}=4.5$ Hz; 3- and 4-OH), 3.55 (1H, m; 3-H), 7.36 (2H, dd; 11- and 12-H), 7.89 (1H, d, $J=2$ Hz; 14-H). The mother liquors (30 ml) were evaporated to give oil whose crystallization from hexane–acetone yielded colorless prisms (13) (0.7 g).

**Methyl 13-Isopropyl-4,7-dioxo-3,4-seco-16-nor-podocarpa-8,11,13-trien-3-oate (17)**——a) A mixture of oxo diol (13) (70 mg), $Pb(OAc)_4$ (130 mg) and $K_2CO_3$ (30 mg) in dry benzene (7.0 ml) was heated at 40—50° for 5 hr. The precipitates were filtered off and the filtrate was worked-up in the usual way. The resulting light yellow oil (46 mg) from the acidic fraction was methylated with $CH_2N_2$–ether to give light yellow oil (46 mg). The oil was chromatographed on silica gel (5.0 g) to give colorless oil (17) (28 mg) in benzene–AcOEt (100:1) eluate. Mass Spectrum: Calcd. for $C_{20}H_{26}O_4$ ($M^+$, *m/e*): 330.1831. Found: 330.1825. $t_R=9.5$ (220°). IR ($CCl_4$): 1742, 1720, 1688. NMR: 1.27 (6H, d, $J=7$ Hz; $CHMe_2$), 1.43 (3H, s,; 10-Me), 2.20 (3H, s; COMe), 3.48 (3H, s; COOMe), 7.26 (2H, dd; 11- and 12-H), 7.83 (1H, d, $J=2$ Hz; 14-H).

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[12] C. Djerassi, H. Wolf, and E. Bunnenberg, *J. Am. Chem. Soc.*, **84**, 4552 (1962).

[13] On addition of $D_2O$ one of them was disappeared.

[14] On addition of $D_2O$ this signal was disappeared.

The neutral fraction gave light yellow oil (22 mg) which was not further examined. IR ($CCl_4$): 2700, 1730, 1720, 1686.

b) To a solution of oxo diol (**13**) (100 mg) in dioxane (8.0 ml) was added a solution of $HIO_4 \cdot 2H_2O$ (100 mg) in $H_2O$ (0.3 ml). After the reaction mixture was allowed to stand for 5 hr at room temperature, it was diluted with $H_2O$ and extracted with benzene. The usual work-up gave light yellow oil (100 mg) as a neutral fraction. $Rf=0.59$ (benzene:AcOEt=1:1). IR ($CCl_4$): 2720, 1730, 1720, 1685.

A solution of the resulting oil (100 mg) in acetone (5.0 ml) was oxidized with $KMnO_4$ (20 mg) in acetone–$H_2O$ (10:1) solution in the presence of $MgSO_4$ (30 mg). The resulting acidic compound (30 mg) was methylated with $CH_2N_2$–ether in the usual way. This compound was identical with **17** which was prepared by $Pb(OAc)_4$ oxidation of **13** by comparison of IR spectra and $t_R$ values.

**3α,4β-Dihydroxy-13-isopropyl-16-nor-5β-podocarpa-8,11,13-triene (14)**——a) To a solution of **13** (100 mg) in dry ether (10 ml) was added a mixture of $LiAlH_4$ (25 mg) and $AlCl_3$ (180 mg) in dry ether (10 ml) and the reaction mixture was refluxed for 11 hr. Then the same amount of $LiAlH_4$–$AlCl_3$ in ether was newly added, and refluxing was continued for 7 hr. The usual work-up gave the colorless crystals (90 mg), which were chromatographed on silica gel (10 g) to give colorless crystals (70 mg) in benzene:AcOEt (7:3) eluate. Its recrystallization from hexane–acetone gave colorless needles (**14**), mp 123—124°. *Anal.* Calcd. for $C_{19}H_{28}O_2$: C, 79.12; H, 9.78. Found: C, 78.96; H, 9.51. $Rf=0.35$ (benzene:AcOEt=1:1). $t_R=2.1, 2.7$ (245°), (10:1). IR ($CCl_4$): 3600, 3450. NMR: 0.55 (3H, s; 4-Me), 1.08 (3H, s; 10-Me), 1.25 (6H, d, $J=7$ Hz; $CHMe_2$), 3.56 (2H,[14] b, $W_{h/2}=12$ Hz; 3- and 4-OH), 3.40 (1H, b, $W_{h/2}=14$ Hz; 3-H), 6.82 (1H, s), 7.00 (2H, s) (aromatic protons).

b) A solution of **13** (700 mg) in benzene (30 ml) was added to a mixture of Zn–Hg (prepared from Zn (6.0 g), $HgCl_2$ (0.6 g) and 27% HCl aq. (19 ml)) in 12.5% HCl aq. (10.4 ml). After the reaction mixture was stirred for 70 min at 80—85°, benzene layer was separated and water layer was extracted with AcOEt. The work-up in the usual way gave colorless semi-solid (720 mg), which was chromatographed on silica gel (45 g). Colorless crystals (290 mg) resulted from benzene–AcOEt (9:1—7:3) eluate were recrystallized from hexane–acetone to give colorless needles (**14**), mp 128—129°. IR ($CCl_4$): 3600, 3450. $Rf=0.3$ (benzene:AcOEt=4:3). $t_R=4.9, 6.1$ (220°) (1:1).

**Methyl 13-Isopropyl-4-oxo-3,4-seco-16-nor-5β-podocarpa-8,11,13-trien-3-oate (18)**——To a solution of diol (**14**) (1.82 g) in dioxane (40 ml) was added a solution of $HIO_4 \cdot 2H_2O$ (3.5 g) in $H_2O$ (7 ml). The reaction mixture was left standing for 1 hr at room temperature, and then diluted with $H_2O$ and extracted with benzene. The usual work-up gave a light yellow oil (**16**) (1.6 g). IR ($CCl_4$): 2700, 1730. The oil was instantly oxidized in acetone (100 ml) with 7.5% $KMnO_4$ in acetone–$H_2O$ (1:1) solution under ice-cooling until $KMnO_4$ was not exhausted. The resulting acidic oil (1.0 g) was methylated with $CH_2N_2$–ether. A part of the oil (850 mg) was chromatographed on silica gel (70 g) to give colorless crystals (320 mg) in benzene–AcOEt (100:1) eluate, whose recrystallization from hexane–acetone gave colorless needles (**18**), mp 82°. *Anal.* Calcd. for $C_{20}H_{28}O_3$: C, 75.91; H, 8.92. Found: C, 75.68; H, 8.95. IR ($CCl_4$): 1740, 1712. NMR: 1.23 (6H, d, $J=7$ Hz; $CHMe_2$), 1.36 (3H, s; 10-Me), 2.18 (3H, s; COMe), 3.50 (3H, s; COOMe), 6.1—7.2 (3H, m; 11-, 12-, and 14-H).

**Epimerisation of 5β-Oxo Ester (18) with 5% KOH-MeOH to 19**——After 5β-oxo ester (**18**) (35 mg) was allowed to stand in 5% KOH–MeOH (4 ml) for 3 days at room temperature, the mixture was diluted with sat. NaCl aq., acidified with 10% HCl aq. and then extracted with ether. The work-up in the usual way yielded oil, which was methylated with $CH_2N_2$–ether to give oil (38 mg). $t_R=3.5, 4.4$ (1:2), (5β-oxo ester: $t_R=5.0$) (220°). $Rf=0.47, 0.42$ (5β-oxo ester; $Rf=0.42$) (benzene:AcOEt=6:0.2). Its purification by pre TLC (benzene:AcOEt=90:5) gave two fractions; Colorless oil (10 mg) ($Rf=0.47$) whose structure was not yet defined, and colorless oil (**19**) ($Rf=0.42$). Mass Spectrum: Calcd. for $C_{20}H_{28}O_3$ ($M^+$, $m/e$): 316.2039. Found: 316.2053. IR ($CCl_4$): 1740, 1735 (sh), 1710, 1700 (sh). NMR: 1.23 (6H, d, $J=7$ Hz; $CHMe_2$), 1.26 (3H, s; 10-Me), 2.17 (3H, s; COMe), 3.54 (3H, s; COOMe), 6.76—7.18 (3H, m; 11-, 12-, and 14-H).

**Favorskii Rearrangement of 5β-Oxo Ester (18)**——To a solution of 5β-oxo ester (**18**) (110 mg) in AcOH (3 ml) was added a solution of 48% HBr (2 drops) and $Br_2$ (120 mg) in AcOH (1 ml). After the reaction mixture was stirred for 1 hr at room temperature and then at 40° for 1 hr, it was diluted with $H_2O$ and extracted with ether. The work-up in the usual way gave yellow oil, to which 3% KOH–MeOH (3 ml) was added. The solution was refluxed for 1.5 hr, then diluted with $H_2O$ and extracted with ether. The water layer was acidified with 10% HCl aq. and extracted with ether. Ether extract gave a light yellow oil (110 mg), which was methylated with $CH_2N_2$–ether as usual to give light yellow oil (110 mg). $t_R=8.0$ (217°). $Rf=0.58, 0.44$ (benzene:AcOEt=6:0.2). Separation of mixed oil by pre TLC (benzene:AcOEt=90:3) gave two fractions: colorless oil (**20**) (40 mg) ($Rf=0.58$). Mass Spectrum: Calcd. for $C_{21}H_{28}O_4$ ($M^+$, $m/e$): 344.1988. Found: 344.2002. IR ($CCl_4$): 1740, 1730 (sh), 1638, 1618. NMR: 1.26 (6H, d, $J=7$ Hz; $CHMe_2$), 1.33 (3H, s; 10-Me), 3.48, 3.68 (each 3H, s; 3- and 15-COOMe), 5.79 (1H, bs, $W_{h/2}=4$ Hz; 4-H), 6.80—7.30 (3H, m; 11-, 12-, and 14-H), and colorless oil (**21**) (27 mg) ($Rf=0.44$). IR ($CCl_4$): 1740, 1735 (sh).

When left in the atomosphere, the former (**20**) was converted to **21** and the latter (**21**) was smoothly converted to other compound ($Rf=0.13$), which was purified by pre TLC (benzene:AcOEt=90:3) to give colorless oil (22). Mass Spectrum: Calcd. for $C_{20}H_{26}O_5$ ($M^+$, *m/e*): 358.1780. Found: 358.1788. IR ($CCl_4$): 1742, 1663.

**Favorskii Rearrangement of 5α-Oxo Ester (19)**——5α-Oxo ester (**19**) (155 mg) was treated in the same manner as 5β-oxo ester (**18**). The resulting yellow oil (134 mg) was methylated with $CH_2N_2$–ether in usual way to give yellow oil. *Rf*=0.58, 0.44 (benzene:AcOEt=6: 0.2). $t_R$=8.0 (217°). IR ($CCl_4$): 1740, 1735 (sh). Its physical constants (*Rf*, $t_R$ value and IR-spectrum) were identified with those of the mixture consisting of **20** and **21** prepared from 5β-oxo ester (**18**).

**Dimethyl 13-Isopropyl-3,4-seco-16-nor-5β-podocarpa-8,11,13-trien-3,15-dioate (23)**——A solution of mixed diester (**20** and **21**) (370 mg) in AcOH (13 ml) was shaken in the presence of Pt (140 mg as $PtO_2$) under hydrogen stream until hydrogen absorption was ceased (about 2 hr). The work-up gave colorless oil (360 mg), consisting of two components ($t_R$=5.6, 6.4 (1: 2.5) (220°)) (350 mg), which was chromatographed on silica gel (25 g) to give colorless oil (**23**) (100 mg) in benzene:AcOEt (100: 1) eluate. Mass Spectrum: Calcd. for $C_{21}H_{30}O_4$ ($M^+$, *m/e*): 346.2144. Found: 346.2184. $t_R$=6.4 (220°). IR ($CCl_4$): 1740. NMR: 1.24 (6H, d, *J*=7 Hz; $CHMe_2$), 1.32 (3H, s; 10-Me), 3.56, 3.66 (each 3H, s; 3- and 15-COOMe), 6.80—7.35 (3H, m; 11-, 12- and 14-H).

**13-Isopropyl-3-oxo-15,16-dinor-5β-podocarpa-8,11,13-triene (25) *via* β-Oxo Ester (24) and Its Enolate Mixture**——Diester (**23**) (100 mg) in dry ether (1 ml) was added to a ether solution (7 ml) of $(C_6H_5)_3CNa$ (prepared from 1% Na–Hg (10 g), $(C_6H_5)_3CCl$ (290 mg) and dry ether (9 ml)). After standing for 18 hr at room temperature, the reaction mixture was acidified with AcOH and diluted with ether. The ether solution was treated with the usual way to give yellow neutral oil (295 mg), whose pre TLC (benzene:AcOEt =100: 3) gave colorless semi-crystals (46 mg), *Rf*=0.40 (benzene:AcOEt=6: 0.3). IR ($CCl_4$): 3600—2400, 1655, 1610 (enol ester), 1750, 1720 (oxo ester).

A solution of the resulting crystals (46 mg) in 10% KOH–MeOH (4 ml) was refluxed for 2 hr. After work-up as usual, the neutral fraction gave a light yellow oil (45 mg) consisting of two components. *Rf*= 0.36, 0.26 (benzene:AcOEt=100: 3). One (*Rf*=0.26) of the fractions gave a colorless oil (**25**) (15 mg). Mass spectrum: Calcd. for $C_{18}H_{24}O$ ($M^+$, *m/e*): 256.1827. Found: 256.1836. IR ($CCl_4$): 1717. NMR: 1.25 (6H, d, *J*=7 Hz; $CHMe_2$), 1.36 (3H, s; 10-Me), 6.86—7.40 (3H, m; 11-, 12- and 14-H). CD (*c*=0.113, MeOH) $[\theta]^{16}$ (nm): −1129 (295), −3162 (265) (negative maximum).