Chem. Pharm. Bull. 24(7)1497—1501(1976)

UDC 547,913.6.04 : 547.914.2.04

Conversion of Dehydroabietic Acid into a Steroid Skeleton: Formation of the D-Ring. II[1]

Akira Tahara (the late),[2a] Yoshihiro Harigaya, and Masayuki Onda[2b]

Rikagaku Kenkyusho (The Institute of Physical and Chemical Research)[2a] and School of Pharmaceutical Sciences, Kitasato University[2b]

(Received September 12, 1975)

Methyl 14-oxo-5α,8β,9α-podocarp-15-oate (**4**) is synthesized from methyl 13-isopropyl-7-oxopodocarpa-5,8,11,13-tetraen-15-oate (**5**) by combination of the following processes: nitration at the 14-position; conversion of the nitro group into the hydroxy group; deisopropylation; reductions of the enone function and C ring; oxidation of the 14-hydroxy group to the oxo group.

In previous papers[3] we reported the conversion of dehydroabietic acid (**1**, R=H) derived from *l*-abietic acid into the C-aromatized steroid (**2**). This is the ABC→D type synthesis of steroid and the first case that the isopropyl group in the C ring is efficiently utilized to form the D ring. However, since synthesis of the steroid possessing the 13-methyl group by this procedure is considered to be difficult, other synthetic approaches are necessary for this objective. Several groups[4] reported the syntheses of the steroidal D ring possessing no methyl group at the 13-position from methyl 12-methoxypodocarpa-8,11,13-trien-16-oate. An intermediate, methyl 12-oxopodocarp-13-en-16-oate (**3**), in the procedure reported by Wheeler, *et al.*[4c] is considered to be a compound suitable for insertion of the methyl group at the 13-position. On the other hand, the 14-oxo compound is also expected to be a key intermediate for synthesis of the steroid possessing the 13-methyl group. In this paper we report synthesis of methyl 14-oxopodocarp-15-oate (**4**) from methyl 13-isopropyl-7-oxopodocarpa-5,8,11,13-tetraen-15-oate (**5**) obtained from **1** (R=H).[5]

For the purpose of obtaining the ketone (**4**), it is necessary to combine properly the following processes: regioselective nitration at the 14-position; conversion of the nitro group into an O-functionalized group; reduction of the C ring.

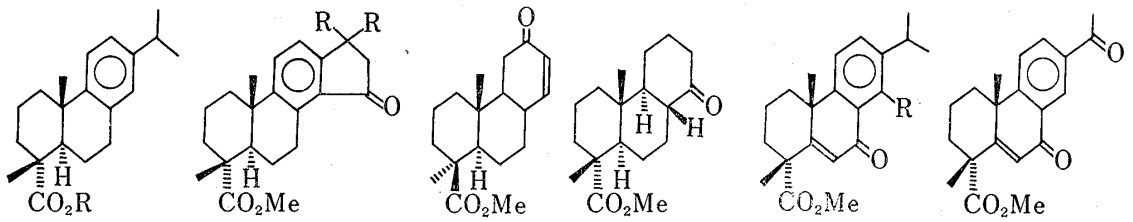
Nitration of **1** (R=Me) was reported to result in the formation of a mixture of isomers.[6] One of us (A.T.) found that the nitration of **5** occurred regioselectively at the 14-position to give the nitro compound (**6**).[7] We followed this procedure and found that besides **6**, the ketone (**7**) was isolated as minor product. The ketone (**7**) is deduced to form probably by oxidation of **5** with nitric acid. Reduction of **6** with tin/hydrochloric acid afforded the amine (**8**) along with a small amount of the amine (**9**) possessing no methoxycarbonyl group. Considering the fact that the hydrolysis of **5** gave the phenacylidene (**10**),[8] the 4-methyl group in **9** may be α. The chemical shifts of the 4- and 10-methyl groups in **9** are similar to those in **10** reported.

1) This paper constitutes Part XLIII of Diterpenoids by A. Tahara and co-workers. Part XLII: M. Shimagaki and A. Tahara (the late), *Chem. Pharm. Bull.* (Tokyo), **24**, 1209 (1976).
2) Location: *a*) *Wako-shi, Saitama 351, Japan*; *b*) *Minato-ku, Tokyo 108, Japan.*
3) A. Tahara, M. Shimagaki, M. Itoh, Y. Harigaya, and M. Onda, *Chem. Lett.*, **1974**, 651; *idem*, *Chem. Pharm. Bull.* (Tokyo), **23**, 3189 (1975).
4) *a*) R.H. Bible, Jr., *C.A.*, **51**, 5838 (1957); *b*) B.R. Davis and W.B. Watkins, *Tetrahedron*, **24**, 2165 (1968); *c*) D.M.S. Wheels and P.R. Witt, *J. Org. Chem.*, **37**, 4211 (1972).
5) E. Wenkert, R.W.J. Carney, and C. Kaneko, *J. Am. Chem. Soc.*, **83**, 4440 (1961).
6) W. Campbell and M. Morgana, *J. Am. Chem. Soc.*, **63**, 1838 (1941); E. Ochiai and M. Ohta, *Yakugaku Zasshi*, **74**, 203 (1954); E.S. Hansen and H.H. Zeiss, *J. Am. Chem. Soc.*, **77**, 1643 (1955).
7) A. Tahara, H. Akita, and Y. Ohtsuka, *Chem. Pharm. Bull.* (Tokyo), **22**, 1547 (1974).
8) J.W. Huffman, *J. Org. Chem.*, **35**, 478 (1970).

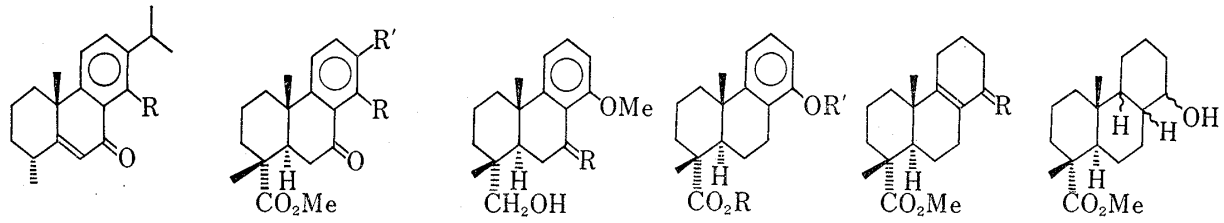
NII-Electronic Library Service

Treatment of a solution of **8** in methanol containing conc. sulfuric acid with sodium nitrite gave **5** (27%), the phenol (**11**) (18%), and the ether (**12**) (38%). The presence and position of the hydroxyl group in **11** are confirmed by the infrared (IR) and nuclear magnetic resonance (NMR) spectra. Structure of **12** is established by the fact that methylation of **11** with dimethyl sulfate gave **12**. Treatment of a solution of **8** in pyridine with a solution of sodium nitrite in sulfuric acid afforded **11** quantitatively. Hydrogenation of **11** over Adams' platinum in acetic acid gave the phenol (**13**), the A/B *trans* configuration of which was proved on the basis of structure of the ether (**16**) obtained from **13** (*vide infra*). The phenol (**13**) was methylated with dimethyl sulfate to give the ether (**14**) which was identified with methyl 14-hydroxy-13-isopropyl-7-oxo-5α-podocarpa-8,11,13-trien-15-oate prepared by another route[9] by the IR and NMR spectra.

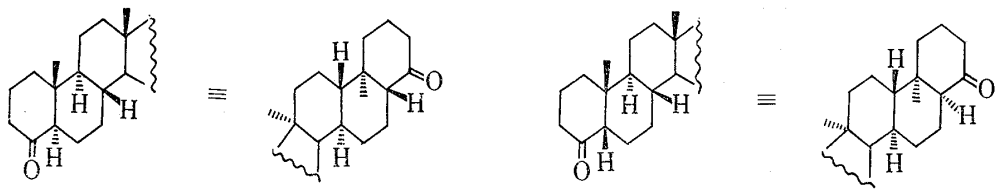
Deisopropylation of **13** afforded the phenol (**15**).[10] The circular dichroism (CD) curve of the ether (**16**) derived from **15** shows the same pattern as that of methyl 13-isopropyl-7-oxo-5α-podocarpa-8,11,13-trien-15-oate (**17**),[11] indicating the α configuration at the 5-position (see Experimental). The Birch reduction of **16**, on the contrary to expectation, gave two carbinol (**18**) and (**19**) whose structures were supported by the IR and NMR spectra. A



1 **2** : R=H, Me **3** **4** **5** : R=H **7**
6 : R=NO_2
8 : R=NH_2
11 : R=OH
12 : R=OMe



9 : R=NH_2 **13** : R=OH, R′=iso-Pr **18** : R=H_2 **20** : R=H, R′=Me **21** : R=H_2 **24**
10 : R=H **14** : R=OMe, R′=iso-Pr **19** : R=O **22** : R=Me, R′=H **23** : R=O
15 : R=OH, R′=H
16 : R=OMe, R′=H
17 : R=H, R′=iso-Pr



25 **26**

Chart 1

9) A. Tahara and H. Akita, *Chem. Pharm. Bull.* (Tokyo), **23**, 1976 (1975).
10) A. Tahara and H. Akita, *Chem. Pharm. Bull.* (Tokyo), **23**, 1984 (1975).
11) P.F. Ritchie, T.F. Sanderson, and L.F. McBurney, *J. Am. Chem. Soc.*, **76**, 723 (1954).

NII-Electronic Library Service

modified Birch reduction and subsequent esterification of the acid (**20**), which was derived from **16** by the Huang-Minlon reduction, provided the Δ^8 compound (**21**) and phenol (**22**) in a comparable amount in stead of the desirable compound (**23**).

The phenol (**22**), which was prepared from **15** by the Huang-Minlon reduction and subsequent esterification,[12] was hydrogenated over ruthenium oxide in ethanol gave the carbinol (**24**) displaying the IR bands at 3450 (OH) and 1727 cm^{-1} (COOMe). The gas–chromatography (GLC) exhibits that **24** is a mixture of two isomers in an approximate ratio of 1:1. The ketone (**4**) was obtained by treatment of **24** with the Jones' reagent. The presence of the carbonyl group in **4** is confirmed by the IR spectrum (CCl_4) showing the band at 1714 cm^{-1} in addition of the one at 1728 cm^{-1} (COOMe). The CD curve of **4** shows the negative Cotton effect ($[\theta]^{28}$—8293). Since the 5α-4-keto (**25**) and 5β-4-keto steroid (**26**) display the negative (—7700) and positive Cotton effect (+250),[13] respectively, **4** can be assigned to possess the 5α, 8β, 9α configuration.

Experimental

Melting points were determined on a micro hot-stage and are not corrected. IR spectra were taken on a JASCO IR-G. NMR spectra were measured with a Varian T-60 (60 MHz) and a JNM-4H-100 (100 MHz). Mass spectra were recorded on a JEOL TMS-OlS. CD curves were taken on a JASCO J-20. GLC was carried out with a Shimadzu GC-3AF. A glass column of 2 m × 4 mm was packed with 1.5% OV-17 on Shimalite W (80—100 meshes). Operating temperature was 240°.

Methyl 13-Isopropyl-14-nitro-7-oxopodocarpa-5,8,11,13-tetraen-15-oate (6) and Methyl 13-Acetyl-7-oxopodocarpa-5,8,11,13-tetraen-15-oate (7)——To a cold solution of the phenacylidene (**5**) (600 mg) in conc. H_2SO_4 (4 ml) was added dropwise a solution of HNO_3 (*d*, 1.53)–conc. H_2SO_4 (1: 1) (10 ml) with cooling and stirring over 15 min. The reaction mixture was stirred for 1 hr, poured onto ice-water, and then extracted with ether. The ethereal residue (590 mg) was purified by combination of recrystallization from chloroform–hexane and chromatography on neutral Al_2O_3 (grade III, 30 g; benzene) to give **6** (296 mg) as colorless needles of mp 205—208°. The IR ($CHCl_3$) and NMR ($CDCl_3$) were superimposed on those described in lit.[7] The eluate of benzene–ethyl acetate (25: 1, v/v) of above chromatography gave **7** (50 mg), recrystallization of which gave light yellow prisms of mp 129—130° from ether–hexane. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1727 (COOMe), 1684 (13-CO), 1653 (C_7=O). NMR ($CDCl_3$): δ 8.64 (d, *J* 2 Hz, 14-H), 8.21 (q, *J* 8.5 and 2 Hz, 12-H), 7.61 (d, *J* 8.5 Hz, 11-H), 6.22 (s, 6-H), 3.73 (s, COOMe), 2.66 (s, 13-COMe), 1.66 (s), 1.56 (s) (4β- and 10β-Me). *Anal.* Calcd. for $C_{20}H_{22}O_4$: C, 73.60; H, 6.79. Found: C, 73.16; H, 6.74.

Methyl 14-Amino-13-isopropyl-7-oxopodocarpa-5,8,11,13-tetraen-15-oate (8) and 14-Amino-13-isopropyl-16-norpodocarpa-5,8,11,13-tetraen-7-one (9)——To a solution of **6** (1.07 g) in methanol (15 ml) was added Sn powder (1.0 g) and conc. HCl (10 ml). After refluxed for 3 hr, the reaction mixture was poured onto ice-water, made alkaline with 20% aq. KOH, and extracted with ether. The ethereal residue (1.02 g) was chromatographed on basic Al_2O_3 (70 g). The benzene–hexane (1: 1, v/v) eluate gave an oil (80 mg) which was crystallized from hexane to give **9** (30 mg) as yellow crystals of mp 128.5—129°. IR ν_{max}^{film} cm^{-1}: 3440, 3280 (NH_2), 1645 (CO). NMR (CCl_4): δ 6.78 (b, 14-NH_2),[14] 7.12 (d, *J* 8 Hz), 6.58 (d, *J* 8 Hz) (11- and 12-H), 6.03 (d, *J* 2 Hz, 6-H), 2.74 (sept, *J* 7 Hz, C<u>H</u>Me_2), 1.44 (s, 10β-Me), 1.26 (d, *J* 7 Hz, CH<u>Me</u>$_2$), 1.19 (d, *J* 6.5 Hz, 4α-Me). *Anal.* Calcd. for $C_{19}H_{25}ON$: C, 80.52; H, 8.89; N, 4.94. Found: C, 80.73; H, 8.94; N, 4.80. The benzene eluate afforded **8** (700 mg) as yellow oil. IR ν_{max}^{film} cm^{-1}: 3470, 3300 (NH_2), 1730 (COOMe), 1640 (CO). NMR ($CDCl_3$): δ 6.79 (b, 14-NH_2),[14] 7.25 (d, *J* 8 Hz), 6.69 (d, *J* 8 Hz) (11- and 12-H), 6.00 (s, 6-H), 3.69 (s, COOMe), 2.87 (sept, *J* 7 Hz, C<u>H</u>Me_2), 1.60 (s), 1.49 (s) (4β- and 10β-Me), 1.26 (d, *J* 7 Hz), 1.21 (d, *J* 7 Hz) (CH<u>Me</u>$_2$). Mass Spectrum: M^+, *m/e* 341.199. Calcd. for $C_{21}H_{27}O_3N$: M, 341.199.

Reaction of the Amine (8) with Sodium Nitrite——a) To a solution of **8** (56 mg) and conc. H_2SO_4 (0.5 ml) in abs. methanol (5 ml) was added $NaNO_2$ (100 mg) with cooling. Stirring was continued for 30 min with cooling and for 15 min at room temperature. After addition of urea (100 mg), the reaction mixture was refluxed for 30 min and evaporated *in vacuo*, extracting with ether. The ethereal residue (52 mg) was purified by pre. TLC[15] (silica gel plates, 0.35 mm; benzene: ethyl acetate=24:1, v/v). The zones with *Rf* 0.69, 0.54, and 0.36 gave **11** (10 mg, 18%), **5** (15 mg, 27%), and **12** (21 mg, 38%), respectively. **11**: Oil. IR ν_{max}^{film} cm^{-1}: 3600—2300 (OH), 1732 (COOMe), 1638 (CO). NMR (CCl_4): δ 12.92 (s, 14-OH),[14] 7.21 (d, *J* 8 Hz), 6.77 (d, *J* 8 Hz) (11- and 12-H), 5.92 (s, 6-H), 3.71 (s, COOMe), 3.33 (sept, *J* 7 Hz, C<u>H</u>Me_2), 1.61 (s), 1.50 (s) (4β- and

12) This procedure improved the yield of **22** compared to that described in lit.[10]
13) P. Crabbé, "Optical Rotatory Disparsion and Ciurcular Dichroism in Organich Cemistry," Holden-Day, San Francisco, 1965.
14) On addition of D_2O this signal disappeared.
15) Preparative thin-layer chromatography.

NII-Electronic Library Service

10β-Me), 1.23 (d, *J* 7 Hz), 1.19 (d, *J* 7 Hz) (CHMe$_2$). Mass Spectrum: M$^+$, *m/e* 342.187. Calcd. for $C_{21}H_{26}O_4$: M, 342.183. **12**: Colorless prisms, mp 108—108.5° (from ether–hexane). IR ν_{max}^{film} cm^{-1}: 1730 (COOMe), 1658 (CO). NMR ($CDCl_3$): δ 7.42 (d, *J* 8 Hz), 7.24 (d, *J* 8 Hz) (11- and 12-H), 6.07 (s, 6-H), 3.83 (s, 14-OMe), 3.70 (s, COOMe), 3.41 (sept, *J* 7 Hz, CHMe$_2$), 1.54 (s), 1.63 (s) (4β- and 10β-Me), 1.25 (d, *J* 7 Hz), 1.20 (d, *J* 7 Hz) (CHMe$_2$). *Anal.* Calcd. for $C_{22}H_{28}O_4$: C, 74.13; H, 7.92. Found: C, 73.86; H, 8.03. **5** was identified with an authentic sample by the IR and NMR spectra.

b) A solution of **8** (600 mg) in pyridine (8 ml) was added dropwise to a cold solution of $NaNO_2$ (800 mg) in 70% H_2SO_4 (25 ml). Treatment of the reaction mixture as mentioned above gave an oil (580 mg) which was identified as **11** by TLC, IR and NMR spectra.

Methyl 13-Isopropyl-14-methoxy-7-oxopodocarpa-5,8,11,13-tetraen-15-oate (12) from the Phenol (11)——A mixture of **11** (90 mg), Me_2SO_4 (0.8 ml), and K_2CO_3 (800 mg) in dry acetone (10 ml) was refluxed for 50 hr. After filtration and removal of solvent *in vacuo*, the resulting residue was taken up in ether to give an oil (98 mg) whose pre. TLC (silica gel plates, 0.4 mm; benzene: ethyl acetate=100: 3, v/v) gave **12** (63 mg) as colorless prisms of mp 107.5—108.5° (from ether–hexane). This compound was identified with the ether (**12**) mentioned above by mixed mp, TLC, IR, and NMR spectra.

Methyl 14-Hydroxy-13-isopropyl-7-oxo-5α-podocarpa-8,11,13-trien-15-oate (13) and Its 14-Methyl Ether (14)——A solution of **11** (450 mg) in acetic acid (14 ml) was shaken with H_2 over Pt black obtained from PtO_2 (90 mg) for 1 hr. The work-up gave an oil (480 mg) whose chromatography (silica gel, 40 g) gave **13** (420 mg) as oil from the benzene–ethyl acetate (100: 1, v/v) eluate. IR ν_{max}^{film} cm^{-1}: 3650—2200 (OH), 1725 (COOMe), 1625 (CO). NMR (CCl_4): δ 12.87 (s, 14-OH),[14] 7.28 (d, *J* 8 Hz), 6.67 (d, *J* 8 Hz) (11- and 12-H), 3.65 (s, COOMe), 3.30 (sept, *J* 7 Hz, CHMe$_2$), 1.33 (s), 1.26 (s) (4β- and 10β-Me), 1.23 (d, *J* 7 Hz), 1.20 (d, *J* 7 Hz) (CHMe$_2$).

The Ether (**14**): **14** was prepared from **13** in 49% yield by the procedure mentioned for **12**. Colorless needles, mp 106—107° (from ether–hexane). IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1730 (COOMe), 1685 (CO). NMR (CCl_4): δ 7.26 (d, *J* 8 Hz), 6.95 (d, *J* 8 Hz) (11- and 12-H), 3.77 (s, 14-OMe), 3.63 (s, COOMe), 3.39 (sept, *J* 7 Hz, CHMe), 1.32 (s), 1.21 (s) (4β- and 10β-Me), 1.21 (d, *J* 7 Hz), 1.51 (d, *J* 7 Hz) (CHMe$_2$). *Anal.* Calcd. for $C_{22}H_{30}O_4$: C, 73.71; H, 8.44. Found: C, 74.00; H, 8.39.

Methyl 14-Hydroxy-7-oxo-5α-podocarpa-8,11,13-trien-15-oate (15) and Its Methyl Ether (16)——To a solution of **13** (390 mg) in dry benzene (18 ml) was added $AlCl_3$ (3.7 g) with cooling. After stirring for **16** hr at room temperature, the reaction mixture was poured onto ice-water and extracted with ether. The ethereal residue (330 mg) was chromatographed on silica gel (30 g) to give **15** (280 mg) as oil from the benzene–ethyl acetate (50: 1, v/v) eluate. Its IR (film) and NMR (CCl_4) spectra were superimposed on those described in lit.[10]

The Ether (**16**): **16** was prepared in 62% yield by the procedure mentioned for **12**. Colorless crystals, mp 112—113° (from ether–hexane). IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1730 (COOMe), 1683 (CO). NMR (CCl_4): δ 7.24 (t, *J* 8 Hz, 12-H), 6.78 (q, *J* 8 and 2 Hz), 6.69 (q, *J* 8 and 2 Hz) (11- and 12-H), 3.79 (s, 14-OMe), 3.61 (s, COOMe), 1.30 (s), 1.17 (s) (4β- and 10β-Me). CD (*c*=0.38, methanol)[16] $[\theta]^{25}$ (mμ): +11642 (331) (positive maximum), 0 (286), −14760 (255) (negative maximum). *Anal.* Calcd. for $C_{19}H_{24}O_4$: C, 72.13; H, 7.65. Found: C, 72.32; H, 7.63.

14-Methoxy-5α-podocarpa-8,11,13-trien-15-ol (18) and 14-Methoxy-7-oxo-5α-podocarpa-8,11,13-trien-15-ol (19)——A solution of **16** (160 mg) in tetrahydrofuran (10 ml) was added dropwise to a mixture of Li (140 mg) and Al powder (1 mg) in liq. NH_3 (20 ml) over 10 min with stirring and cooling on a dry ice/acetone bath. The reaction mixture, to which abs. *t*-butanol (2 ml) was added, was stirred for 3 hr with cooling. After addition of ethanol (2.5 ml) and removal of liq. NH_3, the remaining residue was worked-up to give an oil (130 mg) whose pre. TLC (silica gel, 0.35 mm; benzene: ethyl acetate=3: 1, v/v) gave **18** (47 mg) and **19** (28 mg) from the zones with *Rf* 0.73 and 0.17, respectively. **18**: Colorless crystals, mp 113—114.5° (from ether–hexane). IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3650 (OH). NMR (CCl_4): δ 6.97 (t, *J* 8 Hz, 12-H), 6.70 (q, *J* 8 and 2 Hz), 6.42 (q, *J* 8 and 2 Hz) (11- and 13-H), 3.74 (s, 14-OMe), 3.31 (d, *J* 11 Hz, 15-H$_A$), 3.02 (d, *J* 11 Hz, 15-H$_B$), 2.13 (s, OH),[14] 1.81 (s), 0.79 (s) (4β- and 10β-Me). Mass Spectrum: M$^+$, *m/e* 274.194. Calcd. for $C_{18}H_{26}O_2$: M, 274.193. **19**: Colorless needles, mp 164—166° (from ether–hexane). IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3480 (OH), 1665 (CO). NMR (CCl_4) (100 MHz): δ 7.38 (t, *J* 8 Hz, 12-H), 6.91 (q, *J* 8 and 1 Hz), 6.73 (q, *J* 8 and 1 Hz) (11- and 13-H), 3.75 (s, 14-OMe), 3.49 (d, *J* 11 Hz, 15-H$_A$), 3.11 (d, *J* 11 Hz, 15-H$_B$), 2.40 (OH),[14] 1.19 (s), 0.93 (s) (4β- and 10β-Me). Mass Spectrum: M$^+$, *m/e* 288.174. Calcd. for $C_{18}H_{24}O_3$: M, 288.173.

14-Methoxy-5α-podocarpa-8,11,13-trien-15-oic Acid (20)——A mixture of **16** (90 mg), KOH (300 mg), and $N_2H_4 \cdot 2H_2O$ (0.2 ml) in diethylene glycol (5 ml) was stirred for 1 hr at 120—130°. After addition of KOH (200 mg) and removal of $N_2H_4 \cdot 2H_2O$ *in vacuo*, the reaction mixture was stirred for 2 hr at 210—230° and then diluted with H_2O, extracting with chloroform. The H_2O layer was acidified with 10% HCl and extracted with ether to give a solid (85 mg) of mp 190—195° whose recrystallization from methanol–H_2O gave **20** (36 mg) as colorless prisms of mp 211—214°. IR ν_{max}^{KBr} cm^{-1}: 3600—2250 (COOH), 1690 (COOH). NMR (CCl_4): δ 9.82 (b, COOH),[14] 6.91 (t, *J* 7 Hz, 12-H), 6.66 (q, *J* 7.5 and 2 Hz), 6.41 (q, *J* 7.5 and 2 Hz) (11- and 13-H),

16) CD of **17** (*c*=0.43, methanol) $[\theta]^{25}$ (mμ): +11823 (321) (positive maximum), 0 (309), −10679 (295) (negative maximum).

NII-Electronic Library Service

3.68 (s, 14-OMe), 1.23 (s), 1.16 (s) (4β- and 10β-Me). *Anal.* Calcd. for $C_{18}H_{24}O_3$: C, 74.97; H, 8.39. Found: C, 74.77; H, 8.38.

Methyl 5α-Podocarp-8-en-15-oate (21) and Methyl 14-Hydroxy-5α-podocarpa-8,11,13-trien-15-oate (22)——To a mixture of **20** (100 mg), abs. *t*-amyl alcohol (1.4 ml), and $EtNH_2$ (20 ml) was added Li (110 mg) with stirring and then abs. *t*-amyl alcohol (1.5 ml) was added after reflux for 1 hr. The reaction mixture was refluxed for additional 1 hr and dissolved in H_2O, extracting with chloroform. The H_2O layer was acidified and extracted with ether to give an oil (90 mg). The oily compound (90 mg) was treated with diazomethane and purified by pre. TLC (silica gel plates, 0.4 mm; benzene: ethyl acetate=20: 1, v/v) to give **21** (30 mg) and **22** (47 mg) from zones with *Rf* 0.75 and 0.40, respectively. **21**: Colorless crystals, mp 65—70°. IR ν_{max}^{film} cm^{-1}: 1727 (COOMe). NMR (CCl_4): δ 3.62 (s, COOMe), 1.50 (s), 1.30 (s) (4β- and 10β-Me). Mass Spectrum: M^+, *m/e* 276.209. Calcd. for $C_{18}H_{28}O_2$: M, 276.209. **22**: Colorless prisms, mp 154—155° (from chloroform–hexane). The IR (KBr) and NMR ($CDCl_3$) spectra were superimposed on those described in lit.[9]

Methyl 14-Hydroxy-5α-podocarpa-8,11,13-trien-15-oate (22) from the Phenol (15)——A mixture of **15** (160 mg), KOH (400 mg), and $N_2H_4 \cdot 2H_2O$ (0.4 ml) in diethylene glycol (6 ml) was treated by the procedure mentioned for **20** to give an acidic compound (150 mg) which was converted with diazomethane into **22** (80 mg), colorless crystals, mp 145—148° (from ether–hexane).

Methyl 14-Oxo-5α,8β,9α-podocarp-15-oate (4)——A solution of **22** (85 mg) in ethanol (10 ml) was hydrogenated over RuO_2 (30 mg) at 150 atm and 60°. The work-up gave **24** (90 mg) whose GLC showed two peaks at t_R 4.9 and 5.5 in an approximate ratio of 1: 1. IR ν_{max}^{film} cm^{-1}: 3450 (OH), 1727 (COOMe). To a solution of **24** (90 mg) in acetone (4 ml) was added the Jones' reagent (0.2 ml) with stirring. The reaction mixture was stirred for 1.5 hr, diluted with H_2O and extracted with ether. The ethereal residue (91 mg) was chromatographed on basic Al_2O_3 (9 g) using benzene–hexane (2: 1, v/v) as solvent to afford **4** (41 mg), recrystallization of which gave colorless plates of mp 148.5—150° from ether–hexane. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1728 (COOMe), 1714 (CO). NMR (CCl_4) (100 MHz): δ 3.61 (s, COOMe), 1.11 (s), 0.93 (s) (4β- and 10β-Me). CD (c=0.50, methanol) $[\theta]^{28}$ (mμ): −8293 (286) (negative maximum), *Anal.* Calcd. for $C_{18}H_{28}O_3$: C, 73.94; H, 9.66. Found: C, 73.93; H, 9.65.

NII-Electronic Library Service