199. Akira Tahara, Ken-ichi Hirao, and Yasuhiko Hamazaki :
Diterpenoids. VII.[*1] Study on Catalytic Hydrogenations
of Methyl 9-Oxo-10-hydroxypodocarpa-5,7,10,13-
tetraen-16-oate Enantiomer Type Compounds.[*2]

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In the preceding communication,[1] catalytic hydrogenations of compounds having α-substituted α,β-unsaturated ketone group such as methyl 9-oxo-10-hydroxypodocarpa-5,7,10,13-tetraen-16-oate enantiomer (Ⅳ) and methyl 9-oxo-10-acetoxypodocarpa-5,7,10,13-tetraen-16-oate enantiomer (Ⅲ) in the presence of catalytic amounts of sulfuric acid, were reported. The former compound (Ⅳ) afforded only methyl podocarpa-5,7,10,13-trien-16-oate enantiomer (methyl deoxypodocarpate enantiomer)(Ⅶ) as a sole product, whereas the latter one Ⅲ yielded two kinds of chromatographically separable compounds, methyl 10-β-acetoxypodocarpa-5,7,13-trien-16-oate enantiomer (Ⅷ) in addition of the before described Ⅶ in ratio of 1.9:1. The stereochemical problem on the C_{10}-acetoxy group of Ⅷ was decided as β-configuration on the basis of the reliable evidences,[1] on contrary of the Wenkert's α-assignment[2] for the configuration of C_{10}-acetoxy group of the corresponding nitril (XXV) obtained from XXIV under the same hydrogenation condition.

Concerning this hydrogenation, reinvestigation by gas–liquid chromatographic analyses showed that the hydrogenated mixtures from Ⅳ and Ⅲ were not contaminated with other compounds except the above mentioned compounds.

These noticeable observations on the hydrogenations prompted us to study hydrogenation in absence of sulfuric acid of the same type compounds such as methyl 9-oxo-10-hydroxypodocarpa-5,7,10,13-tetraen-16-oate enantiomer (Ⅳ), the corresponding acid (V) and 7-nitro compound (Ⅵ), from which the respective 9,10-dihydroxy compounds, ester (Ⅸ), m.p. 160~162°, acid (X), m.p. 235.5~238° and amino ester (Ⅺ), m.p. 187~189°, were afforded in excellent yield. Since the acid (X) by methylation and the amino ester (Ⅺ) by deamination were correlated to the ester (Ⅸ), determination of one of their structures lead to decide the structures of all other compounds, which have same skeleton (*i.e.* the same configuration at C_1, C_9, C_{10}, C_{11}, and C_{12}).

At first, our attentions were given to the decision of the stereochemistry on A/B ring fusion of these compounds (Ⅸ), (X), and (Ⅺ) that were conclusively confirmed to have A/B *trans* ring fusion (β C_{11}-H and α C_{12}-Me) by the following reasons. i) Further hydrogenation of the 9,10-hydroxy ester (Ⅸ) in presence of sulfuric acid quantitatively yielded the authentic compound (Ⅶ)[1] having A/B *trans* ring fusion (β C_{11}-H and α C_{12}-Me). ii) Reflux of the 9,10-dihydroxy acid (X) with dilute mineral acid for a few hours gave a neutral oil, whose purity was satisfied by the gas–liquid chromatographic analysis and also, whose structure except stereochemistry was agreeably supported as a hydroxy lactone (Ⅻ) by analysis of its infrared spectrum (IR cm^{-1} (CHCl$_3$): 3600 (OH), 1780 (-$\underline{CO}$-O-)).

*1 Part Ⅵ (as communication) : This Bulletin, **12**, 1121 (1964).

*2 All melting points (except m.m.p.) were measured on the Kofler block and were uncorrected. All NMR spectra were measured at 60Mc. (varian Model A-60) in CDCl$_3$(5~10%) *vs.* Me$_4$Si as internal reference (Authors thank to Dr. K. Takeda and Dr. K. Tori, Shionogi & Co., Ltd., Osaka, for the NMR measurements). All gas–liquid chromatograms were measured by Shimadzu GC-1B (hydrogen flame ionization detector)(Authors thank to Dr. N. Ikekawa, this Institute, Tokyo, for his valuable advice).

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1) A. Tahara, K. Hirao : This Bulletin, **12**, 984 (1964).

2) E. Wenkert, *et al.* : J. Am. Chem. Soc., **80**, 211 (1958); Canad. J. Chem., **41**, 1924 (1963).
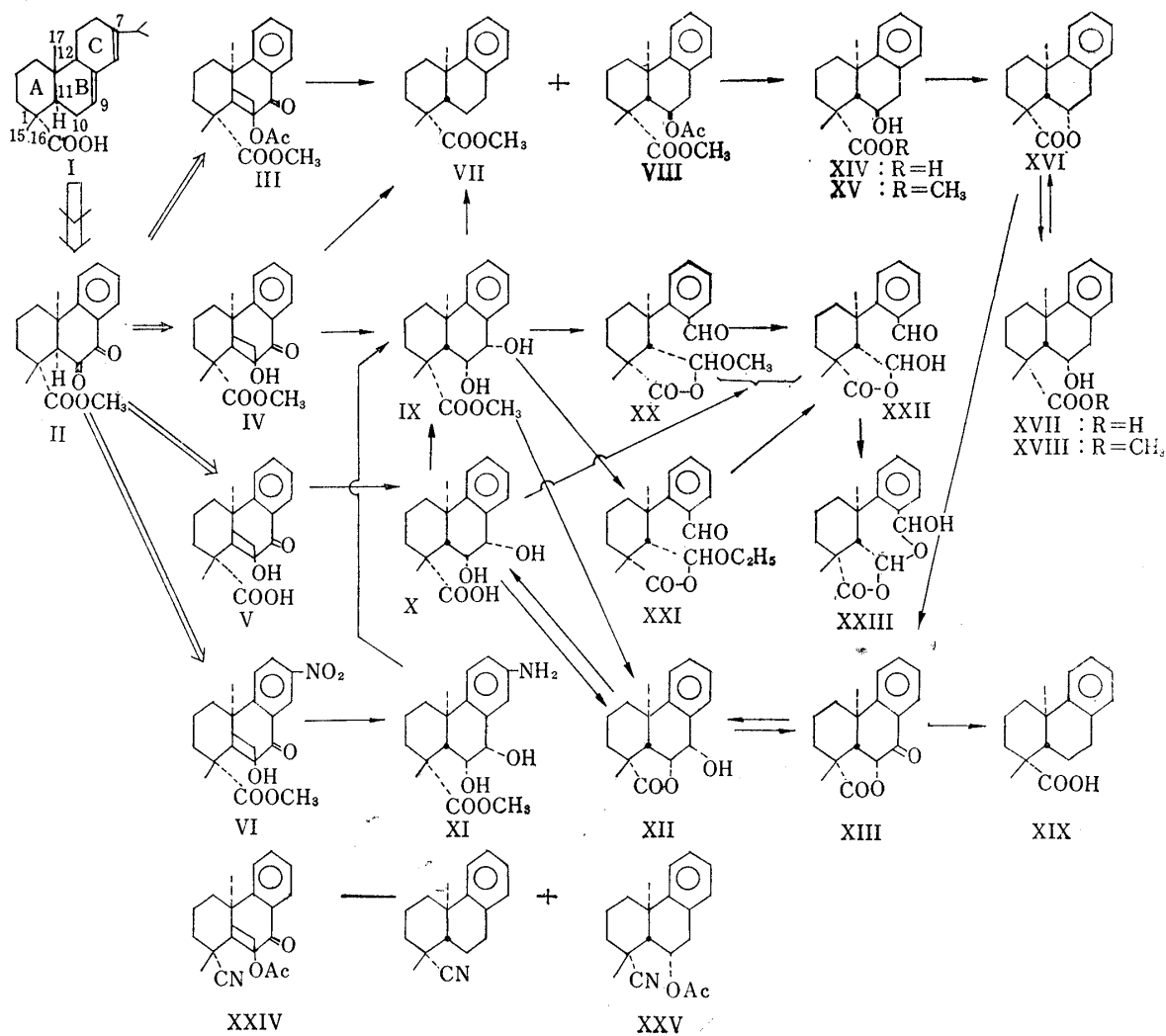
As another preparative way of the hydroxy lactone (XII), it was found that the treatment of the 9,10-dihydroxy ester (IX) on alumina for long times gave XII in company with the recovered ester (IX). Successively, the oily hydroxy lactone (XII) was readily oxidized by chromic acid to keto lactone (XIII), m.p. 163~164.5°, in whose infrared spectrum an absorption at 1705 cm⁻¹ corresponding to α,β-unsaturated ketone newly appeared. The interconnection by the chromic acid oxidation to the keto lactone (XIII) from the lactone (XVI)[1] having the explicit configuration at C_{10}, C_{11}, and C_{12}, as well as the conversion by catalytic hydrogenation from the keto lactone (XIII) to the authentic deoxypodocarpic acid enantiomer (XIX), proved the reliability of the above conclusion on the stereochemistry of A/B ring fusion (*trans*; β C_{11}-H and α C_{12}-Me) of the original dihydroxy ester (IX) and, therefore, of the corresponding acid (X) and the amino ester (XI).

Secondarily, the configuration of the hydroxy group at C_9 and C_{10} of the 9,10-dihydroxy compounds (IX), (X), and (XI) were considered. Nuclear magnetic resonance chemical shifts for methyl group of IX (8.70 τ (C_1-Me), 8.63 τ (C_{12}-Me)) were identical with those of the hydroxy ester (XVIII)[1] (8.70 τ (C_1-Me), 8.63 τ (C_{12}-Me))[1] having α-configuration of the C_{10}-hydroxy group, but not with those of the isomeric hydroxy ester (XV)[1] (8.51 τ (C_1-Me), 8.98 τ (C_{12}-Me))[*1] having β-configuration of the C_{10}-hydroxy group. On the basis of the same thought as in the nuclear magnetic resonance analyses of XV and XVIII,[1] the nuclear magnetic resonance spectrum of IX indicate that its C_{10}-hydroxy group is nearly located to the C_{12}-methyl group, but not to the C_1-methyl group. Also the 9-hydroxy

lactone (XII) was completely regenerated to the original 9,10-dihydroxy acid (X) under the same condition as in the case of that hydroxy lactone (XVI) obtained from the both β-(XIV) and α-hydroxy acid (XVII), was hydrolized only to XVII (α C_{10}-OH), but not to XIV (β C_{10}-OH)[1]. A presumptive α-assignment for the C_{10}-hydroxy group of the 9,10-dihydroxy compounds (IX), (X), and (XI) is not only satisfied by the nuclear magnetic resonance and the chemical observations, but also is not contradictory to the mechanism of the catalytic hydrogenation (1, 2 cis addition of hydrogen to double bond give β C_{11}-H and α C_{10}-OH), which is presumable different from the mechanism of the before reported hydrogenation in presence of sulfuric acid.[1,3]

On the other hand, the configuration of another hydroxy group at C_9 of IX, X, and XI also could be considered as α-configuration, for reasons of that the 9,10-dihydroxy acid (X) was regenerated from the 9-keto lactone (XIII) through the 9-hydroxy lactone (XII) by sodium borohydride reduction, in which hydrogen is attacked from less hindered side (β) of XIII, and successively alkaline hydrolysis. Furthermore confirmation of the above assumption on the configuration of the C_9-hydroxy group (α C_9-OH and α C_{10}-OH are cis each other) was provided from observation that oxidative cleavage of the 9,10-dihydroxy ester (IX) by sodium metaperiodate, which react more easily to cis dihydroxy group than trans one, was proceeded with facility. The trend of the oxidation to the cis dihydroxy compound (IX) is supported by the fact that analogous compounds (XXVI) and (XXVIII) having trans dihydroxy group (β C_9-OH and α C_{10}-OH) were stable to sodium periodate in methanol, whereas its 9-epimers (XXVII) and (XXIX) having cis dihydroxy group were readily cleaved.[4]

In this periodate cleavage, a very interesting fact was found that the cleavage of the 9,10-dihydroxy ester IX in methanol and water solvent afforded a unexpected compound (XX), m.p. 159~161°, having an aldehyde and a methoxy lactone group, in contrast with that the analogous cis dihydroxy ester (XXVII) and (XXIX) were cleaved by sodium periodate to the expected dialdehydes (XXX) and (XXXI) respectively.[4] The structure of XX was
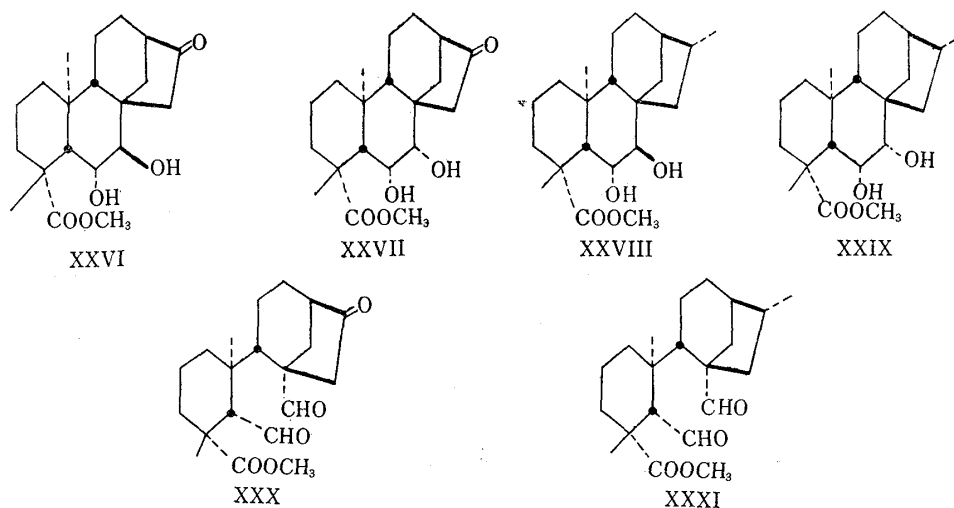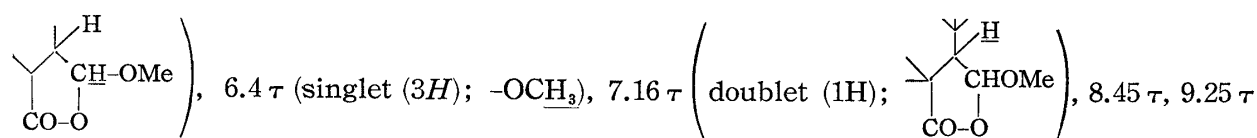

obviously supported by its infrared spectrum (1770 cm^{-1} (-CO-O-), 1675 cm^{-1} (Ph-CO-)),

proton magnetic resonance spectrum (−0.83 τ (singlet (1H); Ph-CHO), 4.58 τ doublet (1H);

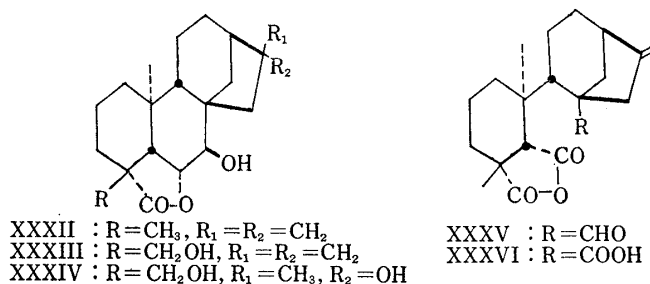3) cf. R. L. Augustin : J. Org. Chem., **23**, 1853 (1958); R. L. Augustin, A. D. Broom : Ibid., **25**, 802 (1960).
4) B. E. Cross, et al. : Tetrahedron, **18**, 451 (1962); J. Chem. Soc., **1963**, 2937, 2944, 3783; 5052.

, 6.4 τ (singlet (3*H*); -OC$\underline{H}_3$), 7.16 τ (doublet (1H);

, 8.45 τ, 9.25 τ

(singlet (3*H*); —C$\underline{H}_3$) and also formation of monosemicarbazone. Preparation of the corresponding ethoxy lactone (XXI), m.p. 169∼171.5°, which was obtained by the same treatment of the 9,10-dihydroxy ester X in ethanol and water solvent, proved that the alkyl group bound to the alkoxy group directly came from the solvent molecule. The both compounds (XX) and (XXI) were acidically hydrolized to the common product (XXII), m.p. 165∼167°, which was also obtained in company with XX in ratio 1:1 from the 9,10-dihydroxy acid (X) by the similar periodate oxidation in methanol and water solvent. Although the hemiacetal type compound (XXII) was completely regenerated from its aq. potassium carbonate solution by acidification, however it was converted by acidification of its aq. sodium hydroxide solution to a new compound (XXIII), m.p. 196∼200°, in whose infrared spectrum an absorption for α,β-unsaturated aldehyde disappeared and for hydroxy group still remained.

In conclusion, the hydrogenation in absence of sulfuric acid of the compounds having α-substituted α,β-unsaturated ketone function such as IV, V and VI afforded only the 9,10-dihydroxy compounds (β C_{11}-H, α C_{10}-OH and α C_9-OH) (IX), (X) and (XI), respectively. These experimental data in addition of the different observations of the hydrogenation in presence of sulfuric acid[1] will give suggestion to consideration of the mechanisms of these hydrogenations.[*4]

Furthermore it must be noted that the structures of our synthetic compounds (IX), (X) and (XI) are considered to have close relationship to the structures of new biosynthetically important metabolites[4] such as hydroxy kaurenolides (XXXII), (XXXIII), (XXXIV), fujenal (XXXV) and fujenoic acid (XXXVI) isolated recently by ICI group from culture filtrates of the fungus *Gibberella fujikuroi*, which is well known as producer of growth promoting substance, gibberellic acid.

XXXII : R=CH$_3$, R$_1$ =R$_2$ =CH$_2$
XXXIII : R=CH$_2$OH, R$_1$ =R$_2$ =CH$_2$
XXXIV : R= CH$_2$OH, R$_1$ =CH$_3$, R$_2$ =OH

XXXV : R=CHO
XXXVI : R=COOH

Experimental

Gas-liquid-chromatographic Analyses of Catalytically Hydrogenated Products (in Presence of Sulfuric Acid) of Methyl 9-Oxo-10-acetoxypodocarpa-5,7,10,13-tetraen-16-oate Enantiomer (III) and Methyl 9-Oxo-10-hydroxypodocarpa-5,7,10,13-tetraen-16-oate Enantiomer (IV).

General Procedure——A solution of the ester (200 mg.) and H$_2$SO$_4$ (2 drops) in AcOEt (20 ml.) was shaken under H$_2$ atmosphere in presence of 10% Pd-C (40 mg.). After absorption of H$_2$ was ceased and then the catalyst was filtered off, the filtrate was washed with 10% aq. Na$_2$CO$_3$, H$_2$O successively, dried over Na$_2$SO$_4$ and evaporated.

i) Gas-liquid-chromatographic analysis of crystals (162 mg.), m.p. 95∼110°, obtained from III (200 mg.) by the above-mentioned procedure, showed only two main peaks in 2.98 min. and 6.23 min. of retention time (1.5% SE-30 on Anakrom (mesh 80∼100), 4 mm. × 1.5 m., 182°) corresponding to methyl podocarpa -5,7,13-trien-16-oate enantiomer (methyl deoxypodocarpate enantiomer) (VII) and to methyl 10-acetoxypodocarpa-5,7,13-trien-16-oate enantiomer (VIII), respectively.

ii) Gas-liquid-chromatographic analysis of crystals (169 mg.), m.p. 110∼130°, obtained from IV (200 mg.) by the above general procedure, showed mainly one peak in 2.98 min. of retention time (1.5% SE-30 on Anakrom. (mesh 80∼100), 4 mm. × 1.5 m., 182°) corresponding to VII in accompany with other small peaks.

[*4] The mechanisms of these hydrogenations in presence or absence of sulfuric acid, will be discussed in detail in Diterpenoids (VI).

Catalytic Hydrogenation of Methyl 9-Oxo-10-hydroxypodocarpa-5,7,10,13-tetraen-16-oate Enantiomer (IV), 9-Oxo-10-hydroxypodocarpa-5,7,10,13-tetraen-16-oic Acid Enantiomer (V), Methyl 7-Nitro-9-oxo-10-hydroxypodocarpa-5,7,10,13-tetraen-16-oate Enantiomer (VI) in Absence of Sulfuric Acid to the Respective 9α,10α-Dihydroxy Compounds (IX), (X) and (XI).

General Procedure——A solution of IV, V or VI (100 mg.) in AcOH (10 ml.) was shaken under H_2 atmosphere in presence of 10% (15% in case of VI) Pd-C (200 mg.). After absorption of H_2 was ceased, the catalyst was filtered off and the filtrate was evaporated in vacuum at room temperature.

i) From IV to IX——The resulted crystals (77 mg.) obtained from IV, whose gas-liquid-chromatogram showed only one peak in 8.63 min. of retention time (1.5% SE-30 on Anakrom. (mesh 80~100), 4 mm. × 1.5 m., 182°), were recrystallized twice from ligroin to give colorless prisms (50 mg.), m.p. 160~162° as analytical sample (IX). Anal. Calcd. for $C_{18}H_{24}O_4$: C, 71.02; H, 7.95. Found : C, 71.12; H, 7.79. IR cm⁻¹(KBr) : 3550, 3480, 1700. NMR (CDCl₃) : 8.70(-CO-C-CH₃), 8.63(—CH₃), 6.21(-COOCH₃).

ii) From V to X——The resulted crystals (85 mg.), m.p. 242~245°, obtained from V, were recrystallized twice from MeOH-H_2O to give colorless prisms, m.p. 235.5~238° as analytical sample (X). Anal. Calcd. for $C_{17}H_{22}O_4$: C, 70.32; H, 7.64. Found : C, 70.41; H, 7.66. IR cm⁻¹(KBr) : 3550, 3470, 1690.

iii) From VI to XI——The resulted crystals (80 mg.), m.p. 166~180°, obtained from VI, were recrystallized twice from ether-petr. ether to give colorless prisms, m.p. 187~189° as analytical sample (XI). Anal. Calcd. $C_{18}H_{25}O_4N$: C, 67.69; H, 7.89; N, 4.39. Found : C, 67.76; H, 7.72; N, 4.40. IR cm⁻¹(KBr): 3480, 3380, 1700, 1610.

Chemical Relation of 9α,10α-Dihydroxypodocarpa-5,7,13-trien-16-oic Acid Enantiomer (X) and Methyl 7-Amino-9α,10α-dihydroxypodocarpa-5,7,13-trien-16-oate Enantiomer (XI) to Methyl 9α,10α-Dihydroxypodocarpa-5,7,13-trien-16-oate Enantiomer (IX). i) Methylation of X to IX——The acid (X, 10 mg.) were methylated with excess CH_2N_2 by the usual method. The resulted crystals were recrystallized from petr. benzin to give colorless prisms, m.p. 160~162°, whose melting point, mixed melting point and IR spectrum were identical with those of the authentic one (IX).

ii) Deamination of XI to IX——To a solution of the amine (XI, 30 mg.) in 10% HCl (1.0 ml.), a solution of sodium nitrite (15 mg.) in H_2O was added under ice-cooling. The reaction mixture was poured into a solution of 17% aq. NaOH (1.1 ml.) and 37% formaline (0.12 ml.). After the reaction mixture was left standing in ice bath for 10 min. and then at room temperature for 1 hr. under stirring, H_2O was added and it was extracted with ether. The ether extract was washed with 10% HCl, then with H_2O and was dried over Na_2SO_4. The solvent was evaporated to give crystals (12 mg.), which were chromatographed on silicic acid-celite (1:1) (1.5 g.) to separate crystals (5 mg.) in petr. ether-ether (4:1) elute. They were recrystallized from ligroin to give colorless prisms, m.p. 154~157°, whose mixed melting point and IR spectrum were identical with those of IX.

Catalytic Hydrogenation of Methyl 9α,10α-Dihydroxypodocarpa-5,7,13-trien-16-oate Enantiomer (IX) in Presence of Sulfuric Acid to Methyl Podocarpa-5,7,13-trien-16-oate Enantiomer (Methyl Deoxypodocarpate Enantiomer) (VII)——A solution of the dihydroxy ester (IX, 50 mg.) in AcOEt (10 ml.) containing H_2SO_4 (0.01 ml.) was shaken under H_2 atmosphere in presence of 10% Pd-Cⱼ(100 mg.). After absorption of H_2 was ceased and the catalyst was filtered off, the filtrate was washed with satd. aq. NaHCO₃, with H_2O successively and was dried over Na_2SO_4. The solvent was evaporated to give crystals (47 mg.), m.p. 130~134°, which were recrystallized from MeOH-H_2O to colorless prisms, m.p. 138~139°, whose mixed melting point and IR spectrum were identical with those of VII.

Synthesis of 9-Oxo-10α-hydroxypodocarpa-5,7,13-trien-16-oic Acid 16→10α-Lactone Enantiomer (XIII) from 9α,10α-Dihydroxypodocarpa-5,7,13-trien-16-oic Acid Enantiomer (X) through 9α,10α-Dihydroxypodocarpa-5,7,13-trien-16-oic Acid 16→10α-Lactone Enantiomer (XII)——After a solution of the acid (X, 180 mg.) and 30% H_2SO_4 (5 ml.) in MeOH (5 ml.) was refluxed for 2 hr., MeOH was evaporated and the residue was extracted with ether. The ether extract was washed with 10% aq. NaOH, with H_2O and was dried over Na_2SO_4 (neutral part). After acidification of the NaOH extract, it was extracted with ether and the ether extract was dried over Na_2SO_4 (acidic part). Evaporation of both the neutral and acidic extracts yielded neutral oil (XII, 137 mg.) and acidic compound (46 mg.), respectively. Gaschromatographic analysis of the former neutral oil (XII), whose IR cm⁻¹(CHCl₃) : 3600, 1780, showed only one peak in 6.32 min. (1.0% SE-30 phase on Chromosorb (60~80 mesh), 4 mm. × 1.5 m., 197°) and in 25.3 min. as trimethyl silyl ether (2.0% nitril-silicon phase on Anachrom A (80~100 mesh), 4 mm. × 1.5 m., 210°), which was produced by treatment of the alcohol (XII) with trimethyl silyl chloride and hexamethyl disilazane in tetrahydrofuran. IR spectrum of the latter acidic crystals was identical with that of the starting diol acid (X).

A solution of the hydroxy lactone (XII, 200 mg.) and CrO₃ (200 mg.) in AcOH (4 ml.) and H_2O (0.08 ml.) was left standing for 20 hr. at room temperature. The reaction mixture was diluted with H_2O and was extracted with ether. The ether extract was washed with 10% aq. KOH, with H_2O successively, was dried over Na_2SO_4 and was evaporated. The resulted crystals (153 mg.) were recrystallized twice from MeOH to give colorless needles (XIII), m.p. 163~164.5°. Anal. Calcd. for $C_{17}H_{18}O_3$: C, 75.53; H, 6.71. Found : C, 75.69; H, 6.70. IR cm⁻¹(KBr) : 1765, 1705.

Lactonization of Methyl 9α,10α-Dihydroxypodocarpa-5,7,13-trien-16-oate Enantiomer (IX) on Neutral Alumina——A mixture of the ester (IX, 30 mg.) and neutral alumina (Woelm, 1.5 g.) in ether (1 ml.) and petr. ether (1 ml.) was left standing at room temgerature for about 10 days. After alumina was separated off, the filtrate was evaporated to give crystals (16 mg.), which were chromatographed on silisic acid–celite (1:1) (3 g.) to give colorless prisms (4 mg.), whose IR spectrum was identical with that of the starting ester (IX), in petr. ether–ether (10:1) elute and oil (10 mg.), whose IR spectrum was identical with that of the hydroxy lactone (XII), in petr. ether–ether (10:2) elute.
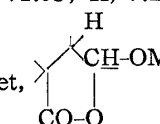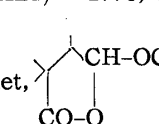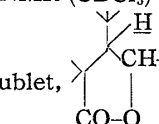
Catalytic Hydrogenation of 9-Oxo-10α-hydroxypodocarpa-5,7,13-trien-16-oic Acid 16→10α-Lactone Enantiomer (XIII) to Podocarpa-5,7,13-trien-16-oic Acid Enantiomer (Deoxypodocarpic Acid Enantiomer) (XIX)——A solution of the keto lactone (XIII, 30 mg.) in AcOH (5 ml.) containing of H_2SO_4 (1 drop) was shaken under H_2 atmosphere in presence of small amounts of 10% Pd–C. After absorption of H_2 was almost ceased, the catalyst was filtrated off and the filtrate was evaporated in vacuum. The residue was diluted with H_2O and was extracted with ether. The ether extract was washed with 10% aq. Na_2CO_3, with H_2O successively, then was dried over Na_2SO_4 and was evaporated. The resulted crystals (30 mg.), m.p. 198~200°, were recrystallized from MeOH–H_2O to give colorless prisms (24 mg.), m.p. 194~197°, whose IR spectrum was identical with that of XIX. *Anal.* Calcd. for $C_{17}H_{22}O_2$: C, 79.03; H, 8.58. Found : C, 78.82; H, 8.43.

Oxidation of 10α-Hydroxypodocarpa-5,7,13-trien-16-oic Acid 16→10α-Lactone Enantiomer (XVI) to 9-Oxo-10α-hydroxypodocarpa-5,7,13-trien-16-oic Acid 16→10α-Lactone Enantiomer (XIII)——A solution of CrO_3 (60 mg.) in AcOH (1 ml.) containing of H_2O (0.1 ml.) was added dropweise to a solution of the lactone (XVI, 30 mg.) in AcOH (2 ml.). The reaction mixture was warmed at 55~60° for 3 hr. and was left standing at room temperature for 2 days. After the excess CrO_3 was decomposed with MeOH, it was evaporated in vacuum, then was diluted with H_2O and was extracted with ether. The extract was washed with 10% aq. Na_2CO_3, with H_2O successively, was dried over Na_2SO_4 and ether was evaporated. Chromatography of the resulted crystals (13 mg.), m.p. 120~137°, on silisic acid–celite (1:1) (2 g.) gave crystals (6 mg.) and the other crystals (6 mg.) in petr. ether–ether (20:1) elute successively. The former crystals were recrystallized from MeOH–H_2O to give colorless needles (4 mg.), m.p. 157~160°, whose mixed melting point and IR spectrum were identical with those of keto lactone (XIII). The latter crystallines were recrystallized from MeOH–H_2O to colorless needles (3 mg.), m.p. 176~178°, whose mixed melting point and IR spectrum were identical with those of the starting material (XVI).

Regeneration of 9α,10α-Dihydroxypodocarpa-5,7,13-trien-16-oic Acid Enantiomer (X) from 9-Oxo-10α-hydroxypodocarpa-5,7,13-trien-16-oic Acid 16→10α-Lactone Enantiomer (XIII) through 9α,10α-Dihydroxypodocarpa-5,7,13-trien-16-oic Acid 16→10α-Lactone Enantiomer (XII)——$NaBH_4$ (150 mg.) were added portionwise to a solution of the keto lactone (XIII, 97 mg.) in MeOH (5 ml.) under stirring. After the reaction mixture was left standing for 2 days at room temperature, 10% HCl (1 ml.) was added and then the solvent was evaporated in vacuum. The residue was diluted with H_2O and was extracted with ether. The ether extract was washed with H_2O, then was dried over Na_2SO_4 and was evaporated. Chromatography of the resulted oil (103 mg.) on silisic acid–celite (1:1) (5 g.) gave oil (61 mg.), whose IR spectrum was identical with that of XII.

A solution of the hydroxy lactone (XII, 32 mg.) in 10% aq. KOH (1 ml.) and MeOH (until complete dissolution) was refluxed for 1.5 hr. After the alkaline reaction solution was extracted with ether, the alkaline layer was acidified and then was extracted with ether. The ether extract from acidified solution was washed with H_2O, then was dried over Na_2SO_4 and was evaporated. The resulted crystals (30 mg.) were recrystallized from MeOH to colorless prisms (21 mg.), m.p. 229~231°, whose mixed melting point and IR spectrum were identical with those of X.

Oxidative Cleavage of Methyl 9α, 10α-Dihydroxypodocarpa-5,7,13-trien-16-oate Enantiomer (IX) with Sodium Metaperiodate. i) In Methanol Solution——To a solution of the dihydroxy ester (IX, 50 mg.) in MeOH (10 ml.), a solution of $NaIO_4$ (300 mg.) in H_2O and then 10% H_2SO_4 (1 ml.) were successively added. After the reaction mixture was left standing at room temperature for 20 hr., it was diluted with H_2O and separated crystals (53 mg.), m.p. 145~155°, were collected. Their chromatography on silisic acid–celite (1:1) (3 g.) gave crystals (38 mg.), m.p. 150~155°, in petr. ether–ether (10:1) elute, which were recrystallized twice from MeOH–H_2O to colorless prisms, m.p. 159~161°, as XX. *Anal.* Calcd. for $C_{18}H_{22}O_4$: C, 71.50; H, 7.33. Found : C, 71.53; H, 7.21. IR cm^{-1}(KBr) : 1770, 1675, 1598. NMR (CDCl$_3$) : −0.83 (singlet,

Ph–C<u>H</u>O), 4.58 (doublet, $\underset{CO-O}{\overset{H}{\underset{|}{\overset{|}{\diagup}}}}$ CH-OMe), 6.4 (singlet, CH-OC<u>H</u>$_3$), 7.16 (doublet, CH-OMe), 8.45, 9.25 (singlet, +C<u>H</u>$_3$).

The aldehyde (XX, 20 mg.) yielded monosemicarbazone (19 mg.), m.p. 228~235° by the usual method. It was recrystallized from MeOH to colorless prisms, m.p. 234~236° as analytical sample. *Anal.* Calcd. for $C_{19}H_{25}O_4N_3$ (as monosemicarbazone) : C, 63.49; H, 7.01; N, 11.69. Found : C, 63.40; H, 6.55; N, 11.50. IR cm^{-1}(KBr) : 3490, 3200, 3130, 1780, 1695, 1575.

ii) In Ethanol Solution——The dihydroxy ester (IX, 50 mg.) in EtOH (8 ml.) were treated with NaIO₄ (300 mg.) as in the case of i). The resulted crystals (40 mg.), m.p. 158∼170°, were recrystallized twice from MeOH to colorless prisms, m.p. 169∼171.5° as analytical sample. *Anal.* Calcd. for C₁₉H₂₄O₄ : C, 72.12; H, 7.65. Found : C, 72.13; H, 7.67. IR cm⁻¹(KBr) : 1760, 1680, 1600.

Reaction of 9α,10α-Dihydroxypodocarpa-5,7,13-trien-16-oic Acid Enantiomer (X) with Sodium Metaperiodate——The acid (X, 50 mg.) in MeOH (8 ml.) were treated with NaIO₄ (300 mg.) as in the case of IX. The resulted crystals (26 mg.), m.p. 125∼135°, were dissolved in 10% aq. K₂CO₃ and it was filtrated. Mixed melting point and IR spectrum of the unsoluble precipitates (9 mg.), m.p. 155∼158°, were identical with those of XX. In other way, acidification of aq. K₂CO₃ filtrate gave crystals (7 mg.), 164∼165°, whose mixed melting point and IR were identical with those of XXII.

Acidic Hydrolysis of the Both Compounds (XX) and (XXI) to Same Product (XXII). **i) Hydrolysis of XX**——A solution of the lactone (XX, 15 mg.) in acetone (1.5 ml.) and 15% H₂SO₄ (1.5 ml.) was refluxed for 4 hr. and then was diluted with H₂O. The separated crystals, m.p. 138∼145°, were recrystallized from MeOH-H₂O to colorless plates, m.p. 165∼167°, as analytical sample of XXII. *Anal.* Calcd. for C₁₇H₂₀O₄ : C, 70.81; H, 6.99. Found : C, 70.61; H, 6.89. IR cm⁻¹(KBr) : 3350, 1745, 1680, 1600.

ii) Hydrolysis of XXI——A solution of the lactone (XXI, 10 mg.) in acetone (1 ml.) and 15% H₂SO₄ (1 ml.) was treated as in the case of i). Separated crystals, m.p. 140∼155°, were recrystallized from MeOH-H₂O to colorless plates, m.p. 165∼167°, whose mixed melting point and IR spectrum were identical with those of XXII obtained from XX.

A solution of the hydrolized product (XXII, 10 mg.) in 10% aq. K₂CO₃ was acidified with conc. HCl. The separated colorless plates, m.p. 163∼165°, whose mixed melting point and IR spectrum were identical with those of starting compound (XXII), were collected.

A soultion of the hydrolized product (XXII, 43 mg.) in 10% aq. KOH was acidified with conc. HCl. The separated crystals (42 mg.), m.p. 200∼203°, were recrystallized from MeOH-H₂O to colorless fine needles (24 mg.), m.p. 196∼200° as analytical sample of XXIII. *Anal.* Calcd. for C₁₇H₂₀O₄ : C, 70.81; H, 6.99. Found : C, 70.40; H, 6.92. IR cm⁻¹(KBr) : 3460, 1742.

Summary

Catalytic hydrogenation of methyl 9-oxo-10-hydroxypodocarpa-5,7,10,13-tetraen-16-oate enantiomer (IV), 9-oxo-10-hydroxypodocarpa-5,7,10,13-tetraen-16-oic acid enantiomer (V) and methyl 7-nitro-9-oxo-10-hydroxypodocarpa-5,7,10,13-tetraen-16-oate enantiomer (VI) in absence of sulfuric acid gave the respective 9α,10α-dihydroxy compounds (IX), (X), and (XI), which are in contrast with the catalytic hydrogenation of methyl 9-oxo-10-acetoxypodocarpa-5,7,10,13-tetraen-16-oate enantiomer (III) and (IV) in presence of sulfuric acid.