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Diterpenoids. XLII.[1] Stereoselective Synthesis of *d*-Phyllocladene from *l*-Abietic Acid[2]

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Stereoselective conversion of *l*-abietic acid (**1**) to *d*-phyllocladene (**16**) was achieved by the use of two carbon units of the isopropyl group in **1** for the formation of its D-ring. Catalytic hydrogenation of methyl 13-methoxycarbonylmethyl-7-oxopodocarpa-8,11,13-trien-15-oate (**2**), derived from **1**, over ruthenium oxide, followed by oxidation, gave stereoselectively methyl 13β-methoxycarbonylmethyl-7-oxopodocarpan-15-oate (**4**), without loss of the 7-oxygen function. Although attempts of cyclization reaction of methyl 7-hydroxy-13β-(2′-hydroxyethyl)-podocarpan-15-oate (**6**) to methyl 15-hydroxy-7-oxo-17-norphyllocladan-18-oate (**7**) were fruitless, the formation of the D-ring from methyl 13β-carboxymethyl-7-oxopodocarpan-15-oate (**5**) was accomplished by polyphosphoric acid–AcOH treatment to give methyl 7,15-dioxo-17-norphyllocladan-18-oate (**9**) in high yield. Selective removal of the 7-oxygen function of **9**, *via* monothioketalization, yielded methyl 15-oxo-17-norphyllocladan-18-oate (**11**), which was further converted to methyl 17-norphylloclad-15-en-18-oate (**14**). Hydroboration of **14**, followed by oxidation, gave methyl 16-oxo-17-norphyllocladan-18-oate (**15**) accompanied with **11**.

We have been studying the chemical transformation to biologically active compounds or their precursors from *l*-abietic acid (**1**), a major component of pine rosin, by using its isopropyl group at the 13-position.[4,5]

In a preceeding paper,[4] we reported the synthesis of *d*-phyllocladene (**16**) and *d*-kaurene (**17**) by the use of a carbon unit of the isopropyl group *via* the Birch reduction of the C-ring, the intramolecular carbenoid reaction of diazoketones and subsequent cleavage of the resulting cyclopropyl ring. This Birch reduction method had nearly no stereoselectivity and gave **16** and **17** in about an equal ratio.

Now, we wish to report the stereoselective synthesis of **16** from **1** by the use of two carbon units of the isopropyl group *via* catalytic hydrogenation over ruthenium oxide, polyphosphoric acid (PPA)–AcOH cyclization and monothioketalization.

We[5] found that the stereoselective hydrogenation of methyl 12-hydroxy-13-isopropyl-podocarpa-8,11,13-trien-15-oate over ruthenium oxide gave methyl 12β-hydroxy-13β-isopropyl-8α-podocarpan-15-oate. Takagi's[6] and Freifelder's[7] groups reported, on the other hand, that the hydrogenation of acetophenone over ruthenium oxide gave 1-cyclohexylethanol. These results may introduce that the hydrogenation of methyl 13-methoxycarbonylmethyl-7-oxopodocarpa-8,11,13-trien-15-oate (**2**) would give methyl 7-hydroxy-13β-methoxycarbonylmethylpodocarpan-15-oate (**3**).

1) Part XLI: H. Akita and A. Tahara (the late), *Chem. Pharm. Bull.* (Tokyo), **24**, 995 (1976).
2) Preliminary communication: M. Shimagaki and A. Tahara (the late), *Tetrahedron Letters*, **1975**, 1715.
3) Location: *Wako-shi, Saitama.*
4) A. Tahara, M. Shimagaki, S. Ohara, and T. Nakata, *Tetrahedron Letters*, **1973**, 1701; A. Tahara (the late), M. Shimagaki, S. Ohara, T. Tanaka, and T. Nakata, *Chem. Pharm. Bull.* (Tokyo), **23**, 2329 (1975).
5) A. Tahara, M. Shimagaki, M. Itoh, Y. Harigaya, and M. Onda, *Chem. Lett.*, **1974**, 651; *idem*, *Chem. Pharm. Bull.* (Tokyo), **23**, 3189 (1975).
6) Y. Takagi, T. Naito, and S. Nishimura, *Bull. Chem. Soc. Japan*, **37**, 585 (1964).
7) M. Freifelder, T. Anderson, Y. Hay NG, and V. Papendick, *J. Pharm. Sci.*, **53**, 967 (1964).

Wenkert's[8] and Herz's[9] groups reported that the 13-formylmethyl-7-oxo compounds having a methyl group at the 13-position gave a D-ring *via* an aldol condensation. The 13-methyl group is an extra carbon in the synthesis of phyllocladene, kaurene, grayanolides and so on. Methyl 15-hydroxy-7-oxo-17-norphyllocladan-18-oate (**7**), having no 13-methyl group, would be obtained from **3** *via* methyl 7-hydroxy-13β-(2'-hydroxyethyl)-podocarpan-15-oate (**6**).

The oxo diester (**2**),[5] prepared from **1**, was used as a starting material. In order to obtain a compound having an oxygen function at the 7-position, **2** was catalytically hydrogenated over ruthenium oxide in EtOH to give **3**. The hydroxy diester (**3**) was oxidized with the CrO_3·pyridine complex in CH_2Cl_2 to give methyl 13β-methoxycarbonylmethyl-7-oxopodocarpan-15-oate (**4**) in 38% yield from **2**. So the hydrogenation of **2** would be performed stereoselectively.

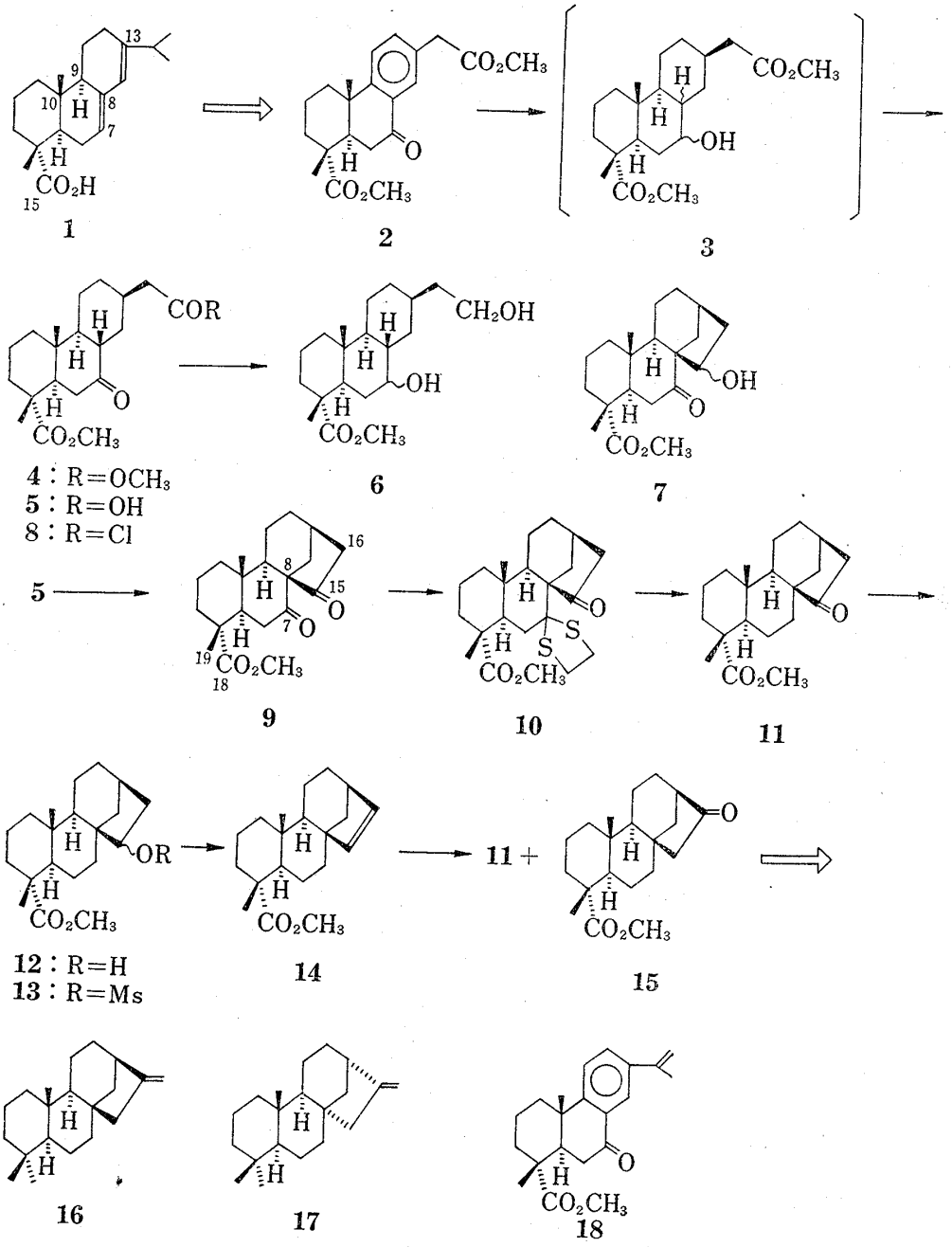

Chart 1

8) E. Wenkert, P.W. Jeffs, and J.R. Mahajan, *J. Am. Chem. Soc.*, **86**, 2218 (1964).
9) W. Herz, A.K. Pinder, and R.N. Mirrington, *J. Org. Chem.*, **31**, 2257 (1966).

The nuclear magnetic resonance (NMR) spectrum provided no signal for the aromatic protons. The infrared (IR) spectrum showed the absorption bands at 1740, 1730 and 1710 cm^{-1} for the carbonyl groups. The optical rotatory dispersion (ORD) curve gave a weak negative Cotton effect, which indicated that the hydrogen at the 8-position possesses a β-configuration, as the hydrogen at the 9-position possesses an α-configuration as mentioned below.[9] A confirmation of the configuration of the 13-position was stated later.

A ring formation was carried out as followed. To apply Wenkert's[8] and modified Herz's[9] methods **4** was converted to **6**. The oxo diester (**4**) was partially hydrolyzed with aq. methanolic KOH to give methyl 13β-carboxymethyl-7-oxopodocarpan-15-oate (**5**) ($\nu_{max}^{CCl_4}$ cm^{-1}: 3670—2250, 1730, 1710, 1705 (shoulder)) in a quantitative yield. The oxo half ester (**5**) was hydroborated to give **6** in 73% yield.[10] The dioxy ester (**6**) was treated with the CrO_3·pyridine complex in CH_2Cl_2 and then with alumina or NaOMe, but no desired cyclization product (**7**) was obtained. An attempts to obtain **7** by Rosenmund reduction of methyl 13β-(chloroformylmethyl)-7-oxopodocarpan-15-oate (**8**), prepared from **5**, followed by the same treatment as above, was also unsuccessful. The compounds having no methyl group at the 13-position could not cause the aldol condensation as mentioned above. Then **5** was treated with BF_3·etherate, with or without solvent (ether or AcOH), or with $(CF_3CO)_2O$ in CF_3CO_2H, which also did not give the desired product.

The oxo half ester (**5**) under PPA–AcOH conditions[11] (100°, 7 hr, stirring), however, caused a desired cyclization to give methyl 7,15-dioxo-17-norphyllocladan-18-oate (**9**), as a sole product. The IR spectrum ($CHCl_3$) showed the absorption bands at 1735, 1725 and 1700 cm^{-1} for the carbonyl groups. It is noticiable that **9**, unlike the compound having a D-ring at the α-side,[8] could be purified by silica gel chromatography. This cyclization reaction was much affected with the proportion of the reagents, moreover the AcOH–free PPA conditions gave a complex mixture. The maximum yield of 72.5% was obtained by a reaction mixture of **5** (181 mg), PPA (9.05 g; prepared from 85% H_3PO_4 (10 ml) and P_2O_5 (25 g)) and AcOH (7.3 ml).

In order to decide the configuration of the D-ring and the hydrogen at the 9-position, **9** was converted to methyl 16-oxo-17-norphyllocladan-18-oate (**15**) whose configuration had been confirmed,[4] *via* methyl 15-oxo-17-norphyllocladan-18-oate (**11**), *i.e.* a selective removal of the 7-carbonyl group and a shift of the remaining carbonyl group from the 15- to 16-position was performed. Fortunately, **9** was converted with excess ethanedithiol in BF_3·etherate to a desired monothioketal (**10**) (δ: 3.20 (s, SCH_2CH_2S); $\nu_{max}^{CHCl_3}$ cm^{-1}: 1720). The 15-carbonyl group did not affect the thioketalization because of a steric hindrance due to a 1,3-diaxial interaction between the 8—15 bond on the D-ring and the 10-methyl group (the 7-carbonyl group was a little hindered so as not to give a ketal with ethyleneglycol in the presence of *p*-TsOH in refluxing abs. C_6H_6). The monothioketal (**10**) was reduced with Raney Ni (W-7) to give **11** in 83% yield from **9**. The IR spectrum showed the absorption band at 1735 and 1730 cm^{-1} for the carbonyl groups. The ORD curve gave a negative Cotton effect, which suggested that the D-ring possesses a β-configuration.[12] The monoxo ester (**11**) was reduced with $NaBH_4$ in EtOH–tetrahydrofuran to give methyl 15-hydroxy-17-norphyllocladan-18-oate (**12**) ($\nu_{max}^{CCl_4}$ cm^{-1}: 3645, 1725) in a quantitative yield. The hydroxy ester (**12**) was mesylated with MsCl in pyridine to give methyl 15-methylsulfonyloxy-17-norphyllocladan-18-oate (**13**), and subsequently treated with γ-collidine to give methyl 17-norphylloclad-15-en-18-oate (**14**) in 69% yield from **12**. The ester (**14**) was hydroborated in the usual manner,[13] followed by oxidation

10) We reported previously a tedious work of the preparation of **5** *via* the protection of the 7-functionality by a nitrate ester.[2]
11) H. Gerlach and W. Müller, *Angew. Chem.*, **84**, 1110 (1972).
12) W. Klyne, *Tetrahedron*, **13**, 29 (1961).
13) *cf.* H.C. Brown and G. Zweifel, *J. Am. Chem. Soc.*, **82**, 3222 (1960); W. Nagata, M. Narisada, T. Wakabayashi, and T. Sugasawa, *J. Am. Chem. Soc.*, **86**, 929 (1964).

with the CrO_3·pyridine complex in CH_2Cl_2 to give a mixture of **15** and **11**. The mixture was conveniently separated by the action of the Girard reagent, as **15** reacted and **11** unreacted with it. The yields of **15** and **11** was 25% and 10%, respectively. The physical constants (mp, mixed mp, gass–liquid chromatography (GLC), IR, NMR, ORD and mass spectrum (MS)) of **15** were completely identical with those of the authentic sample.[4] Then the configuration of the hydrogen at the 9-position is α, and the D-ring possesses a β-configuration. This provides that the configuration of the 13-methoxycarbonylmethyl group of **3** is β. These results are reasonable on the assumption that the hydrogenation over ruthenium oxide of **2** occurred to the α-side, less hindered side. Consequently, as interrelation from **15** to **16** has been published,[4] the stereoselective synthesis of *d*-phyllocladene (**16**) from *l*-abietic acid (**1**), using two carbon units of the 13-isopropyl group, has been accomplished.

The catalytic hydrogenation over ruthenium oxide, with maintaining the functionality at the benzylic position, may be a synthetically useful method. The PPA–AcOH cyclization might be extended to the synthesis of **16** from **1** using three carbon units of the 13-isopropyl group by utilizing methyl 13-isopropenyl-7-oxopodocarpa-8,11,13-trien-15-oate (**18**),[5] derived from **1**, as a starting material and also to the synthesis of other natural products having the D-ring at the same side to the 10-methyl group with no 13-methyl group.

Experimental

Boiling and melting points are uncorrected. Melting points were measured on a micro hot-stage. Retention times (t_R) of GLC were detected by using a glass column (1.5% OV-17 on Shimalite W(80—100 mesh), 4 mm×2.0 m) and N_2 as carrier gas. NMR spectra were measured at 60 MHz in $CDCl_3$ *vs.* Me_4Si as internal reference. ORD were taken with a JASCO MODEL ORD/UV-5 spectrometer. High-resolution mass spectra (high-MS) were taken with a JEOL JMS-01SG spectrometer. Gas chromatography-mass spectra (GC-MS) were taken with a Hitachi model 063 (GLC) and RMS-4 (MS) spectrometer.

Methyl 13β-Methoxycarbonylmethyl-7-oxopodocarpan-15-oate (4) *via* Methyl 7-Hydroxy-13β-methoxycarbonylmethylpodocarpan-15-oate (3)——The oxo diester (**2**)[5] (1.05 g) and ruthenium oxide (0.525 g) in EtOH (26.5 ml) were shaken overnight under 140 kg/cm^2 of H_2 pressure at 50°. After cooling, the catalyst was removed by filtration and washed with ether. Concentration of the combined organic filtrate gave an oil (1.02 g), crude **3**, IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3620, 3480 (b), 1725, 1715.

The oil (1.02 g) in $CaCl_2$–dried CH_2Cl_2 (5.0 ml) was added in one portion under water cooling to the stirred CrO_3·pyridine complex in CH_2Cl_2,[14] prepared from CrO_3 (2.1 g), pyridine (8.0 ml) and CH_2Cl_2 (20 ml), and the mixture was stirred at room temperature for one hr. The reaction mixture was poured onto Florisil (6 g) column and eluted with ether. Removal of the solvent gave an oil (1.22 g), which was chromatographed on Florisil (60 g) with *n*–hexane–ether (1: 8—1: 16) as eluant to give **4** (0.406 g; 38% from **2**), bp 155—160° (bath, 0.015 mmHg). IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1740, 1730, 1710. NMR δ ($CDCl_3$): 1.10, 1.22 (each s, 3H×2, CH_3×2), 3.70 (s, 6H, CO_2CH_3×2). ORD (c=0.0011, dioxane) $[\alpha]^{27}$ (mμ): −123° (313) (trough), 0° (294), +164° (277) (last reading). *Anal.* High-MS Calcd. for $C_{21}H_{32}O_5$ (M^+; *m/e*) 364.2249. Found: 364.2271. 2,4-Dinitrophenylhydrazone: mp 176—177° (AcOEt–EtOH). *Anal.* Calcd. for $C_{27}H_{36}O_8N_4$: C, 59.54; H, 6.66; N, 10.29. Found: C, 59.32; H, 6.62; N, 10.35.

Methyl 13β-Carboxymethyl-7-oxopodocarpan-15-oate (5)——To a solution of **4** (200 mg) in MeOH (4.0 ml) was added water (0.1 ml) and KOH (260 mg), and the mixture was stirred at room temperature for 14 hr. After removal of the solvent at room temperature, ether and water was added. The ether layer was separated off. The residual water layer was washed with ether. The water layer was acidified with conc. HCl and extracted with ether. The ether layer was washed with brine and dried over Na_2SO_4. Removal of the solvent gave a semi crystalline product of **5** (194 mg; quantitative). IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3670—2250, 1730, 1710, 1705 (shoulder). NMR δ ($CDCl_3$): 1.10, 1.23 (each s, 3H×2, CH_3×2), 3.67 (s, 3H, CO_2CH_3).

The half ester (**5**) was treated with ethereal CH_2N_2 to give **4**.

Methyl 7-Hydroxy-13-(2′-hydroxyethyl)-podocarpan-15-oate (6)[10]——To a stirred solution of **5** (60.4 mg) in abs. tetrahydrofuran (4.0 ml) was introduced B_2H_6, generated from a solution of $NaBH_4$ (350 mg) in abs. diglyme (3.0 ml) and that of BF_3·etherate (2.5 ml) in abs. diglyme (2.0 ml),[15] by applying a slight stream of

14) To a KOH–dried pyridine (8.0 ml) was added CrO_3 (2.1 g) with stirring at 10—20°, and the mixture was stirred at room temperature for one hr. Dry petr. ether (5 ml) was added, and the solvent mixture was decanted. The residue was washed five times with dry petr. ether (each 5 ml). The precipitate was dissolved in $CaCl_2$–dried CH_2Cl_2 (20 ml) to give the CrO_3·pyridine complex in CH_2Cl_2.

15) G. Zweifel and H.C. Brown, *Org. React.*, **13**, 1 (1963).

dry N_2 through a generator, at room temperature. After stirring at room temperature for 1 hr and 40 min, water was added cautiously under ice cooling and the mixture was extracted with ether. The extract was washed with 10% Na_2CO_3 solution and brine and dried over Na_2SO_4. Removal of the solvent gave an oil (57.4 mg), which was chromatographed on silica gel (6 g) with *n*-hexane–ether (1: 2—1: 6) as eluant to give **6** (42.4 mg; 73%), bp 165—170° (bath, 0.02 mmHg). IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3630, 3600—3100, 1725. NMR δ ($CDCl_3$): 0.91, 1.20 (each s, 3H×2, CH_3×2), 3.0—3.4 (m, 1H, 7-H), 3.60—3.81 (m, 2H, 2′-H), 3.70 (s, 3H, CO_2CH_3). *Anal.* High-MS Calcd. for $C_{20}H_{32}O_3$ (M^+-18; *m/e*): 320.2351. Found: 320.2336.

Acetylation of **6** with Ac_2O–pyridine gave methyl 7-acetoxy-13-(2′-acetoxyethyl)podocarpan-15-oate as an oil, bp 170° (bath, 0.02 mmHg). IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1740 (shoulder), 1735, 1730 (shoulder). NMR δ($CDCl_3$): 0.91, 1.17 (each s, 3H×2, CH_3×2), 2.05 (s, 6H, $OCOCH_3$×2), 3.65 (s, 3H, CO_2CH_3), 3.96—4.60 (m, 3H, 7- and 2′-H). *Anal.* Calcd. for $C_{24}H_{38}O_6$: C, 68.22; H, 9.07. Found: C, 68.09; H, 8.92.

Reaction of 6 with the CrO_3·pyridine Complex, followed by Alumina Treatment——The diol ester (**6**) (94.2 mg) in $CaCl_2$–dried CH_2Cl_2 (3.5 ml) was added in one portion to the stirred CrO_3·pyridine complex in CH_2Cl_2, prepared from CrO_3 (225 mg), pyridine (2.0 ml) and CH_2Cl_2 (2.0 ml), at 25° under N_2, and the mixture was continued to stir for 15 min. The reaction mixture was poured onto neutral alumina and eluted with ether to give an oil (48.8 mg). The oil was purified by preparative thin-layer chromatography (silica gel; Merck PF_{254}, 20 cm×20 cm×0.5 mm) with *n*-hexane–ether (2: 1; twice elution), but no sign of the desired product (**7**) was obtained (checked by GC-MS and MS).

Reaction of 6 with the CrO_3·pyridine Complex, followed by NaOMe Treatment——The diol ester (**6**) (51.6 mg) in $CaCl_2$–dried CH_2Cl_2 (1.5 ml) was added in one portion under ice cooling to the stirred CrO_3·pyridine complex in CH_2Cl_2, prepared from CrO_3 (100 mg), pyridine (1.0 ml) and CH_2Cl_2 (1.0 ml), and the mixture was stirred for 3 hr (the temperature was raised gradually from 3° to 25° as the ice was melting). The reaction mixture was diluted with ether and it was washed with 10% Na_2CO_3 solution and brine and dried over Na_2SO_4. Removal of the solvent gave an oil (46.3 mg).

To the oil (46.3 mg) was added a solution of NaOMe in abs. MeOH, prepared from Na (90 mg) and abs. MeOH (1.5 ml), with ice cooling under N_2. The mixture was stirred at room temperature under N_2 for 17 hr. Water was added, and the mixture was extracted with ether. The extract was washed with brine and dried over Na_2SO_4. Removal of the solvent gave an oil (15.0 mg), but no sign of **7** was obtained (checked by GC-MS).

Rosenmund Reduction of Methyl 13-(Chloroformylmethyl)-7-oxopodocarpan-15-oate (8), prepared from 5, followed by Alumina Treatment——To a stirred solution of **5** (29.2 mg) in abs. C_6H_6 (1.0 ml) was added $SOCl_2$ (50 μl) in the presence of a trace of pyridine under water cooling. The mixture was stirred at room temperature for 1.5 hr. Removal of the solvent at room temperature gave **8**.

A mixture of **8**, 10% Pd–$BaSO_4$ (30 mg), quinoline-S (30 mg) and abs. xylene (3.0 ml) was refluxed with vigorous stirring under slow stream of H_2 for 5.5 hr. After cooling, the catalyst was removed by filtration and the filtrate was concentrated to give an oil (39.7 mg). The oil was chromatographed on alumina (4 g) with *n*-hexane–ether (3: 1—1: 1) as eluant, but no sign of **7** was obtained (checked by GC–MS).

Rosenmund Reduction of 8, followed by NaOMe Treatment——A mixture of **8**, prepared from **5** (23.8 mg), 10% Pd–$BaSO_4$ (25 mg), quinoline-S (25 mg) and abs. xylene (3.0 ml) was refluxed with vigorous stirring under slow stream of H_2 for 5 hr. After cooling, the catalyst was removed by filtration and the filtrate was concentrated to give an oil (23.5 mg).

To a solution of the oil (23.5 mg) in abs. tetrahydrofuran (1.0 ml) was added NaOMe in abs. MeOH, prepared from Na (30 mg) and abs. MeOH (0.3 ml), under ice cooling and the mixture was refluxed under N_2 for 2 hr. To the reaction mixture was added water and it was extracted with ether. The extract was washed with brine and dried over Na_2SO_4. Removal of the solvent gave an oil (3.0 mg), which gave no sign of **7** (checked by GC-MS).

The water layer was acidified with 10% HCl solution and it was extracted with ether. The extract was washed with brine and dried over Na_2SO_4. Removal of the solvent gave an oil (22.5 mg), which was not further investigated.

Reaction of 5 and Methyl 13-(Acetoxycarbonylmethyl)-7-oxopodocarpan-15-oate[16]——Although attempts of cyclization reaction were carried out as listed in Table I, no desired product[9] was obtained (checked by GC-MS).

Reaction of 5 with PPA in AcOH[11] **to Methyl 7,15-Dioxo-17-norphyllocladan-18-oate (9)**——To a solution of **5** (181 mg) in AcOH (7.3 ml) was added PPA (9.05 g), prepared from 85% H_3PO_4 (10 ml) and P_2O_5 (25 g), at room temperature and the mixture was heated with stirring at 100° for 7 hr. The reaction mixture was poured onto ice water and extracted with ether. The extract was washed with 10% Na_2CO_3 solution and brine and dried over Na_2SO_4. Removal of the solvent gave a crystalline product of **9** (124 mg; 72.5%). A part of **9** was chromatographed on silica gel (50 parts) with *n*-hexane–ether (3: 1—1: 1) to give pure **9**, mp

16) A solution of **5** (100 mg) in Ac_2O (10 ml) was refluxed for 5 hr and then the excess Ac_2O was removed to give methyl 13-(acetoxycarbonylmethyl)-7-oxopodocarpan-15-oate (108.7 mg), IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1825, 1755, 1725, 1710.

Table I. Attempts of Cyclization Reaction of **5** and Its Acid Anhydride

Run	Amount of			Reaction		Product (crude, mg)	
	Material[a] (mg)	Solvent[b] (ml)	Catalyst[c] (ml)	Temperature	Time (hr)	Neutral	Acidic
1	72.7	2.0	1.0	refluxing	13	4.5	64.5
2	78.1	2.5	2.5	refluxing	13	45.1	29.4
3	9.1	nil	1.0	room	8	2.7	7.9
4	100.5	nil	5.0	150°	12	130.4	3.5
				room	18.5		
5	10.0	0.5	0.1	then	then	0.9	9.1
				refluxing	1.5		
6	100.0	20	0.2	water	120	22.5	72.7
7	18.7	1.0	0.02	refluxing	2	1.6	7.2

a) **5** : Run 1—5; the acid anhydride of **5** : Run 6—7
b) Abs. ether : Run 1, 6; purified AcOH[d]: Run 2, 7; CF_3CO_2H : Run 5
c) BF_3·etherate : Run 1—4, 6—7; $(CF_3CO)_2O$: Run 5
d) Guaranteed reagent of AcOH was refluxed in the presence of $KMnO_4$ for 10 hr and distilled. The distillate was dried over P_2O_5 and redistilled to give purified AcOH.

202.5° (sublim.) (C_6H_6–*n*–hexane). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1735, 1725, 1700. NMR δ ($CDCl_3$): 1.05, 1.24 (each s, 3H×2, CH_3×2), 3.67 (s, 3H, CO_2CH_3). *Anal.* Calcd. for $C_{20}H_{28}O_4$: C, 72.26; H, 8.49. Found: C, 72.21; H, 8.55. High-MS Calcd. (M^+; *m/e*): 332.1987. Found: 332.2004.

Methyl 15-Oxo-17-norphyllocladan-18-oate (11) *via* Methyl 7-Ethylenedithio-15-oxo-17-norphyllocladan-18-oate (10)——To a stirred solution of **9** (149.2 mg) in ethanedithiol (1.0 ml) was added BF_3·etherate (1.0 ml) under ice cooling and the mixture was stirred at room temperature for 5.5 hr. Water was added to the reaction mixture and it was extracted with ether. The extract was washed with water, 10% Na_2CO_3 solution and brine and dried over Na_2SO_4. Removal of the solvent gave oily **10** (210.0 mg), IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1720 and $\nu_{max}^{CCl_4}$ cm^{-1}: 1730. NMR δ ($CDCl_3$): 0.90, 1.20 (each s, 3H×2, CH_3×2), 3.20 (s, 4H, SCH_2CH_2S), 3.71 (s, 3H, CO_2CH_3).

A mixture of crude **10** (210.0 mg), Raney Ni (W-7), prepared from Ni–Al (10 g), and EtOH (50 ml) was refluxed with stirring for 9 hr. After removal of the catalyst by filtration, the filtrate was concentrated to give a crystalline product, which was chromatographed on silica gel (1.5 g) with $CHCl_3$ as eluant to give **11** (118.8 mg; 83% from **9**), mp 161° (sublim.) (*n*-hexane). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1720 and $\nu_{max}^{CCl_4}$ cm^{-1}: 1735, 1730. NMR δ ($CDCl_3$): 0.83, 1.17 (each s, 3H×2, CH_3×2), 3.60 (s, 3H, CO_2CH_3). ORD (dioxane) mμ: 326.5 (trough), 319 (peak), 313.5 (trough), 309 (0°), 286 (last reading). *Anal.* Calcd. for $C_{20}H_{30}O_3$: C, 75.43; H, 9.50. Found: C, 75.21; H, 9.48. High-MS Calcd. (M^+; *m/e*): 318.2195. Found: 318.2178.

Methyl 15-Hydroxy-17-norphyllocladan-18-oate (12)——A solution of **11** (57.1 mg) in abs. tetrahydrofuran (4.5 ml) and abs. EtOH (0.75 ml) was stirred with $NaBH_4$ (57.1 mg) at room temperature for 16 hr. The reaction mixture was diluted with ether and it was washed with water and dried over Na_2SO_4. Removal of the solvent gave **12** (57.5 mg; quantitative), mp 148—149.5° (ether–*n*–hexane). IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3645, 1725. NMR δ ($CDCl_3$): 1.06, 1.17 (each s, 3H×2, CH_3×2), 3.67 (s, 3H, CO_2CH_3), 3.92 (d.d, J=5.5 and 10 Hz, 1H, 15–H). *Anal.* Calcd. for $C_{20}H_{32}O_3$: C, 74.96; H, 10.06. Found: C, 75.04; H, 9.89.

Methyl 17-Norphyllocla-15-en-18-oate (14) *via* Methyl 15-Methylsulfonyloxy-17-norphylocladan-18-oate (13)——A mixture of **12** (65.2 mg) and mesyl chloride (0.2 ml) in KOH–dried pyridine (0.5 ml) was left standing at room temperature for 15.5 hr. The reaction mixture was poured onto ice and it was extracted with ether. The extract was washed with water, 10% HCl solution, water, 10% NaOH solution and brine and dried over Na_2SO_4. Removal of the solvent gave a crude mesylate (**13**) (62.5 mg), IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1730.

The crude mesylate (**13**) (62.5 mg) in γ-collidine (2.0 ml) was refluxed for 17.5 hr under N_2. After cooling, the reaction mixture was diluted with ether and it was washed with 10% HCl solution and brine and dried over Na_2SO_4. Removal of the solvent gave a crystalline product (47.4 mg), which was chromatographed on silica gel (5 g) with *n*–hexane–ether (100: 1) as eluant to give **14** (42.3 mg; 69% from **12**), bp 60—70° (bath, 0.06 mmHg). IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1725. NMR δ ($CDCl_3$): 0.78, 1.17 (each s, 3H×2, CH_3×2), 3.66 (s, 3H, CO_2CH_3), 5.75, 5.76 (each s, sum of 2H, 15,16–H). *Anal.* High-MS Calcd. for $C_{20}H_{30}O_2$ (M^+; *m/e*); 302.2246. Found: 302.2260.

Methyl 16-Oxo-17-norphyllocladan-18-oate (15) and 11——To a stirred solution of **14** (42.3 mg) in abs. tetrahydrofuran (6.0 ml) was introduced B_2H_6, generated from a solution of $NaBH_4$ (750 mg) in abs. diglyme (7.5 ml) and that of BF_3·etherate (4.5 ml) in abs. diglyme (4.5 ml),[15] by applying a slight stream of dry N_2 through a generator at room temperature. After stirring for 1.5 hr (total), water (2 ml) was added cautiously. To the mixture was added 15% NaOH solution (4.5 ml) at room temperature, followed by dropwise addition of 30% H_2O_2 solution (4.5 ml), and it was heated with stirring at 40—50° for one hr. After cooling, the reac-

tion mixture was saturated with NaCl and extracted with ether. The extract was washed with brine and dried over Na_2SO_4. Removal of the solvent gave an oil (35.8 mg), IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3640, 1725.

The oil (35.8 mg) in $CaCl_2$-dried CH_2Cl_2 (4.0 ml) was added in one portion under ice cooling to the CrO_3·pyridine complex in CH_2Cl_2, prepared from CrO_3 (155 mg), pyridine (2.0 ml) and CH_2Cl_2 (2.0 ml), and the mixture was stirred for one hr. The reaction mixture was poured onto silica gel (1 g) column and eluted with ether to give a crystalline product (31.7 mg), GLC: **14**: **11**: **15**=1: 2.2: 2.8.

To a solution of the product (31.7 mg) in MeOH (1.0 ml) was added the Girard reagent P (63.5 mg) and AcOH (one drop) and the mixture was refluxed for one hr. The reaction mixture was diluted with water and it was washed with ether. The water layer was acidified with conc. HCl and it was refluxed for 2 hr. The reaction mixture was extracted with ether and the extract was washed with brine and dried over Na_2SO_4. Removal of the solvent gave a crystalline product (14.4 mg), which was chromatographed on silica gel (2 g) with *n*-hexane–ether (7: 1) as eluant to give **15** (11.2 mg; 25% from **14**), mp 171.5—172° (*n*-hexane). Mixed mp 171—172°.[4] IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1745, 1730. GLC (200°) t_R: 4.39 min. NMR δ ($CDCl_3$): 0.91, 1.17 (each s, 3H×2, CH_3×2), 3.62 (s, 3H, CO_2CH_3). ORD (dioxane) mμ: 321 (peak), 313 (trough), 309 (peak), 281 (trough). *Anal.* High-MS Calcd. for $C_{20}H_{30}O_3$ (M^+; *m/e*): 318.2195. Found: 318.2192.

The physical constants (mp, mixed mp, GLC, IR, NMR, ORD, and MS) were identical with those of the authentic sample.[4]

The ethereal washing of the Girard reagent P treatment was washed with brine and dried over Na_2SO_4. Removal of the solvent gave a crystalline product (17.6 mg), which was chromatographed on silica gel (2 g) with *n*-hexane–ether (100: 1) as eluant to recover **14** (4.6 mg; 11%) and with *n*-hexane–ether (20: 1) as eluant to give **11** (4.3 mg; 10% from **14**).