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Diterpenoids. XXX. Reaction of Methyl Dehydroabietate Derivatives with Aluminum Chloride under Effect of Electron-donating Group[1]

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Reactions of methyl dehydroabietate derivatives having electron-donating group at aromatic C-ring with aluminum chloride were examined. It became clear that the reaction proceeded through isomerisation of 9,10-bond and/or deisopropylation and the direction of the reaction is affected by the substituent at the aromatic C-ring. For instance, the reaction of 12-hydroxy ester (**7**) proceeded through both routes while 14-hydroxy ester (**19**) was selectively deisopropylated. Interconversion between *cis*- and *trans*-stereoisomers of deisopropyl ester (*e.g.*, **10**↔**9**) was observed and the former is predominant in the equilibrium.

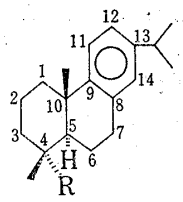
In our studies on the chemical conversion of pine rosin to biologically active compounds, the deisopropylation of dehydroabietic acid (**1**) is important as one of the basic reactions. Ohta's[3] and Wenkert's group[4] reported that the deisopropylation of **1** ($AlCl_3$; 2.25 mol. eq., 30—33°, 3 hr) and **4** ($AlCl_3$; 5.27 mol. eq., reflux, 6 hr) gave the *cis* ester (**2**: 44% and **5**: 39% yield) as a major product and the *trans* ester (**3**: 6% yield and **6**: undiscovered), respectively.

Effect of the substituent at the aromatic C-ring of methyl dehydroabietate derivatives[5] on the deisopropylation offered an attractive problem, and detailed study was made in the present work.

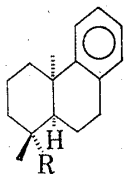
At first, the effect of electron-donating hydroxyl and methoxyl groups at 12- and 14-position was examined. The reaction ($AlCl_3$; 12.4 mol. eq., room temp., 2 hr) of the 12-hydroxy ester (**7**) gave three kinds of the products, 10α-12-hydroxy ester (**8**: 20% yield), mp 164—165.5°, 10β-12-hydroxy-deisopropyl ester (**9**: 38% yield), mp 185—188°, and the known 10α-12-hydroxy-deisopropyl ester[6] (**10**: 34% yield), together with the starting material (**7**: 8% yield). The different point from Ohta's and Wenkert's results was that the *cis* isomer (**8**) with the isopropyl group was isolated.

Structure of the *cis* ester (**8**) was determined from its nuclear magnetic resonance (NMR) spectrum. Signals due to 4- (δ 1.10) and 10-methyl (δ 1.17) were observed in addition to that (δ 1.24; d, J=7.2 Hz) due to the isopropyl methyl, and the pattern belongs to that of methyl deisopropyl-*allo*-dehydroabietate (**11**) having a *cis* A/B-ring juncture.[7] The signal pattern due to the aromatic protons of **8** is the type of 1,2,4,5-substituted benzene and remains the same as in the *trans* isomer (**7**). For a comparison with 10β-12-hydroxy deisopropyl ester (**9**), the authentic sample of **9** was reliably synthesized from methyl deisopropyl-dehydroabie-

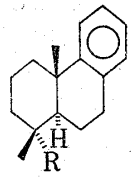
1) Part XXIX: A. Tahara, H. Akita, and Y. Ohtsuka, *Chem. Pharm. Bull.* (Tokyo), **22**, 1555 (1974).
2) Location: *Wako-shi, Saitama-ken, 351, Japan.*
3) M. Ohta and L. Ohmori, *Chem. Pharm. Bull.* (Tokyo), **5**, 91 (1957).
4) E. Wenkert and B.G. Jackson, *J. Amer. Chem. Soc.*, **80**, 211 (1958).
5) Dehydroabietic acid (**1**) and the nitrile (**4**) were used for deisopropylation by Ohta's and Wenkert's group, respectively. In our case, the corresponding esters were used for convenience of the treatment. It is conceivable that these compounds make little difference to the deisopropylation.
6) M. Ohta, *Yakugaku Zasshi*, **77**, 924 (1957).
7) K. Hirao, S. Mitsubayashi, J. Uzawa, A. Tahara, N. Mitomo, and S. Hayashi, *Chem. Pharm. Bull.* (Tokyo), **18**, 2169 (1970).



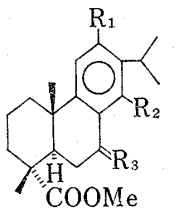
1 : R=COOH
4 : R=CN
31 : R=COOMe



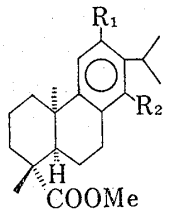
2 : R=COOH
5 : R=CN
11 : R=COOMe



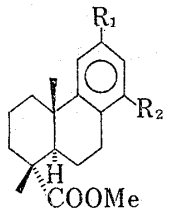
3 : R=COOH
6 : R=CN
12 : R=COOMe



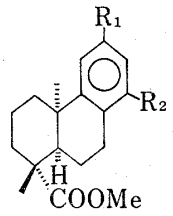
7 : R_1=OH, R_2=H, R_3=H_2
15 : R_1=OMe, R_2=H, R_3=H_2
19 : R_1=H, R_2=OH, R_3=H_2
20 : R_1=H, R_2=OMe, R_3=H_2
21 : R_1=H, R_2=OMe, R_3=O
22 : R_1=H, R_2=OH, R_3=O
23 : R_1=H, R_2=NH_2, R_3=O
24 : R_1=H, R_2=NH_2, R_3=H_2



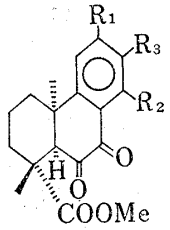
8 : R_1=OH, R_2=H
17 : R_1=OMe, R_2=H
27 : R_1=H, R_2=OMe
32 : R_1=H, R_2=H
33 : R_1=H, R_2=OH



9 : R_1=OH, R_2=H
13 : R_1=Ac, R_2=H
14 : R_1=OAc, R_2=H
18 : R_1=OMe, R_2=H
25 : R_1=H, R_2=OH
34 : R_1=H, R_2=OMe



10 : R_1=OH, R_2=H
16 : R_1=OMe, R_2=H
26 : R_1=H, R_2=OH
28 : R_1=H, R_2=OMe



29 : R_1=OMe, R_2=H, R_3=H
30 : R_1=H, R_2=OMe, R_3=iso-C_3H_7

Chart 1

tate (**12**) by the analogous method (successive treatment of acetylation (**12**→**13**), Baeyer-Villiger oxidation (**13**→**14**), and hydrolysis (**14**→**9**)) to that used in podocarpic acid series.[8]

As to the 12-methoxy ester (**15**), the reaction ($AlCl_3$; 5.30 mol. eq., room temp., 2 hr) proceeded in the same manner and gave 10α-12-methoxydeisopropyl ester[9] (**16**: 18% yield) and an inseparable mixture consisting of the starting material (**15**), 10α-12-methoxy ester (**17**), and 10β-12-methoxy-deisopropyl ester (**18**). After the mixture was demethylated and esterified, the resulting hydroxy esters (**7**: 3% yield, **8**: 7% yield, and **9**: 4% yield) were isolated and confirmed.

For the examination on the effect of electron donating group at 14-position, 14-hydroxy (**19**) and 14-methoxy ester (**20**) were synthesized as follows. 14-Methoxy-7-oxo ester (**21**: 63% yield), mp 98—100°, was obtained in company with the corresponding hydroxy ester[10] (**22**: 13% yield) from 14-amino-7-oxo ester[10] (**23**) previously synthesized by us. The former

8) E. Wenkert and B.G. Jackson, *J. Amer. Chem. Soc.*, **80**, 217 (1958).
9) The ester (**16**) was produced from the known compound[6] (**10**).
10) A. Tahara, H. Akita, and Y. Ohtsuka, *Chem. Pharm. Bull.* (Tokyo), **22**, 1547 (1974).

(**21**) was hydrogenolyzed (H_2-3 kg/cm^2, 10% Pd-C, AcOH-conc.H_2SO_4) to give the aimed 14-methoxy ester (**20**: 89% yield), mp 93—95°, which was also produced from 14-amino ester[11] (**24**). The other requisite compound, 14-hydroxy ester (**19**: 28% yield from **20** and 82% yield from **22**), bp 150° (oil bath)/2×10^{-2} Torr, was obtained by demethylation and esterification of 14-methoxy ester (**20**) or by hydrogenolysis (H_2-3 kg/cm^{-2}, 10% Pd-C, AcOH-conc.H_2SO_4) of 14-hydroxy-7-oxo ester (**22**).

Under a similar condition ($AlCl_3$; 4.96 mol. eq., room temp., 2 hr) as for 12-substituted compounds, the reaction of 14-hydroxy ester (**19**) gave *trans* (**25**: 41% yield), mp 147—149°, and *cis* deisopropyl ester[6] (**26**: 29% yield) in addition to the starting material (**19**: 25% yield).

Although the *trans* isomer (**25**) was isolated in preference to the *cis* (**26**), unlike in the reaction of unsubstituted (**1** and **4**) and 12-substituted ester (**7** and **15**), the *cis* isomer (**26**) was still the major in the reaction equilibrium shown by gas-liquid chromatographic examination to be described later. Structure of the *trans* isomer (**25**) was confirmed by analysis of its NMR spectrum, in which the chemical shift (δ 1.19 and 1.27) due to 4- and 10-methyl groups resembled those of the *trans* standard (**12**: δ 1.22, 1.30).

The reaction of 14-methoxy ester (**20**) ($AlCl_3$; 5.17 mol eq., room temp., 2 hr) showed a similar tendency as that of 12-methoxy ester (**15**). After 10α-14-methoxy ester (**27**: 33% yield), mp 172—172.5°, was separated, the remaining inseparable mixture was demethylated, esterified, and separated. They were identified as the corresponding hydroxy esters, 10β-14-hydroxy deisopropyl ester (**25**: 22% yield), 10α-14-hydroxy deisopropyl ester (**26**: 11% yield) and 10β-14-hydroxy ester (**19**: 11% yield). Structure of the new ester (**27**) was assumed from NMR analysis that the signals (δ 1.12 and 1.21) due to 4- and 10-methyl groups are similar to those of the standard *cis* ester (**11**: δ 1.10, 1.23).

In general, the marked difference in the result of chromic acid oxidation of *trans* and *cis* isomers on A/B ring juncture of dehydroabietic acid derivative, giving 7-oxo and 6,7-dioxo compounds, respectively, is utilized for the detemination of stereochemistry.[12] Thus, the stereochemical evidence of the *cis* isomers (**16** and **27**) assigned earlier was provided by their oxidation to the 6,7-dioxo esters (**29**), oil, and (**30**), mp 160—164°, respectively.

Next attention is called to variation of ratio of the products in dependence of the amount of aluminum chloride. The ratio was detected by gas-liquid chromatography and the result is shown in Table I.

In the gas chromatogram of the reaction product of methyl dehydroabietate (**31**), the peaks due to the usual products (**11** and **12**) were detected under a drastic condition ($AlCl_3$; 4.72—23.6 mol. eq., room temp., 2 hr), but some peaks (50% of sum of peak area) in addition to those peaks were detected under the mild reaction condition ($AlCl_3$; 2.36 mol. eq., room temp., 2 hr). Though indefinite, a structure due to one of the peaks is possibly to be **32**. Chromatographic analysis on the reaction of 12-hydroxy ester (**7**) showed that the *cis* ester (**8**) and *trans*-deisopropyl ester (**9**) decrease and, in contrast, *cis*-deisopropyl ester (**10**) increases according to the amount of aluminum chloride increases. On the other hand, the reaction of 14-hydroxy ester (**19**) was observed in somewhat different manner as shown in Table I. The *cis* isomer (**33**) having an isopropyl group could not be found in any experimental runs. Thus, Chromatographic analysis on the reaction of 12-hydroxy ester (**7**) showed that the *cis* ester it has been proved clearly that the starting ester (**19**) was directly deisopropylated to the *trans* ester (**25**) and then **25** was isomerized to the *cis* (**26**), not through **33** as an intermediate. In equilibrium of the reaction of 12- (**7**) and 14-hydroxy ester (**19**), the respective *cis* (**10** or **26**) and *trans* deisopropyl ester (**9** or **25**) existed only in predominant state of the former isomer over the latter. It becomes noticeable that the reaction of methyl 12- or 14-hydroxy (meth-

11) E. Ochiai and M. Ohta, *Yakugaku Zasshi*, **74**, 203 (1954).
12) U.R. Ghatak, D.K. Datta, and S.C. Ray, *J. Amer. Chem. Soc.*, **82**, 1728 (1960).

TABLE I. Relation between Ratio of Products and Amount of Aluminum Chloride in the Reaction of Methyl Dehydroabietate[a]

Reaction of unsubstituted ester[b] (**31**)

Amount of $AlCl_3$ (mg, mol. eq.)	Product (%)			
	31	*cis*-Deisopropyl(**11**)	*trans*-Deisopropyl (**12**)	Other
100 (2.36)	21	14	15	50
200 (4.72)	0	73	27	0
500 (11.8)	0	74	26	0
1000 (23.6)	0	73	27	0

Reaction of 12-hydroxy ester (**7**)

Amount of $AlCl_3$ (mg, mol. eq.)	Product (%)			
	7	*cis* (**8**)	*trans*-Deisopropyl (**9**)	*cis*-Deisopropyl (**10**)
100 (2.48)	100	0	0	0
200 (4.96)	19	35	32	14
500 (12.4)	16	34	28	22
1000 (24.8)	13.5	29	29.5	28
2000 (49.6)	0	0	38	62

Reaction of 14-hydroxy ester (**19**)

Amount of $AlCl_3$ (mg, mol. eq.)	Product (%)			
	19	*cis*[c] (**33**)	*trans*-Deisopropyl (**25**)	*cis*-Deisopropyl (**26**)
100 (2.48)	100	0	0	0
200 (4.96)	60	0	40	0
1000 (24.8)	19	0	53	28
2000 (49.6)	0	0	32	68

Reaction of 12-methoxy ester (**15**)

Amount of $AlCl_3$ (mg, mol. eq.)	Products (%)		
	15	*cis*-Isopropyl[c] (**17**) or/and *trans*-deisopropyl[c] (**18**)	*cis*-Deisopropyl (**16**)
1000 (25.86)	22	64	14
2000 (51.73)	0	31	69

Reaction of 14-methoxy ester (**20**)

Amount of $AlCl_3$ (mg, mol. eq.)	Products (%)		
	20	*cis*-Isopropyl (**27**) or/and *trans*-deisopropyl[c] (**34**)	*cis*-Deisopropyl[c] (**28**)
100 (2.59)	100	0	0
200 (5.17)	76	24	0
500 (12.93)	42	54	4
1000 (25.86)	30	61	9
2000 (51.73)[d]	5	38	57
1000 (25.86)[e]	0	42	58

a) general procedure: A solution of the ester (100 mg), the object of the experiments, in ab. benzene (10 ml) was stirred at room temp. for 2 hr with $AlCl_3$ and the reaction mixture was treated usually as in the experimental part. Ratio (%) of the resulting conponents was measured by their peak area (height × width of half height) in gas-liquid chromatogram (260—280°).

b) The condition reported by Ohta for **1**[3]: $AlCl_3$ (2.25 mol. eq.), 30—33°, 3 hr and that reported by Wenkert for **4**[4]: $AlCl_3$ (5.27 mol. eq.), reflux, 6 hr.

c) The samples for gas chromatographic analyses were prepared as follows: *cis*-14-Hydroxy ester (**33**) was obtained (BBr_3–CH_2Cl_2 and then CH_2N_2) from the corresponding 14-methoxy ester (**27**) synthesized in pure state.
The samples of *cis*-12-methoxy (**17**), *trans*-12-methoxy-deisopropyl (**18**), *trans*-14-methoxy deisopropyl (**34**), and *cis*-14-methoxy deisopropyl ester (**28**) were obtained (Me_2SO_4–K_2CO_3) from the corresponding hydroxy esters (**8**, **9**, **25**, and **26**), respectively.

d) The case was carried out for 40 hr.

e) The case was carried out at 70°.

oxy)dehydroabietate (*e.g.* **7** and **19**) is much slower than that of the corresponding unsubstituted ester (**31**).

In gas chromatographic examination of 12- (**15**) and 14-methoxy ester (**20**), retention times of the *cis* ester and the *trans*-deisopropyl ester (**17** and **18**; **27** and **34**, respectively) were unfortunately identical and, thus, the reaction result could not be precisely analyzed. However, it is quite possible that the reaction proceeds through either of the same courses as in the case of hydroxy esters (**7** and **19**).

From the observation mentioned above (Table I), the mutual conversion between *cis*- and *trans*-deisopropyl ester (*e.g.*, 12-hydroxy derivatives **9**⇄**10**) should be considered. The experiments were attempted to prove this assumption and the results are shown in Table II. Ratios of *trans* and *cis* isomer in the mixture obtained by the treatment of *trans* (**12**, **9**, and **25**) and the corresponding *cis* ester (**10**) and (**26**) are almost the same values. Two examples (**8** and **27**) shown in the lower line of Table II make it clear that methyl *cis* dehydroabietate derivative newly isolated could also be deisopropylated to give an equilibrium mixture of *cis* and *trans* esters (*e.g.*, **8**→**9**+**10**). The *cis*-ester with an isopropyl group (*e.g.*, **8**) is regarded as the reaction intermediate.

Table II. Chemical Conversion between Methyl Dehydroabietate Derivatives having *trans* and *cis* A/B-ring Juncture[a)]

Starting material	Ratio of products
trans Deisopropyl ester (**11**)	*trans* (**11**): *cis* (**12**)=28:72
trans-12-Hydroxy-deisopropyl ester (**9**)	*trans* (**9**): *cis* (**10**)=35:65
cis-12-Hydroxy-deisopropyl ester (**10**)	*trans* (**9**): *cis* (**10**)=35:65
trans-14-Hydroxy-deisopropyl ester (**25**)	*trans* (**25**): *cis* (**26**)=39:61
cis-14-Hydroxy-deisopropyl ester (**26**)	*trans* (**25**): *cis* (**26**)=31:69
cis-12-Hydroxy ester (**8**)	*trans* (**9**): *cis* (**10**)=36:64
cis-14-Methoxy ester (**27**)	*trans* (**34**): *cis* (**28**)=40:60

a) general procedure: A solution of the ester (50 mg) in ab.benzene (5 ml) was stirred at room temp. for 24 hr with $AlCl_3$ (1 g) and the reaction mixture was treated usually. Ratio (%) of the resulting components was measured by their peak area (heigh × width of half height) in gas-liquid chromatogram.

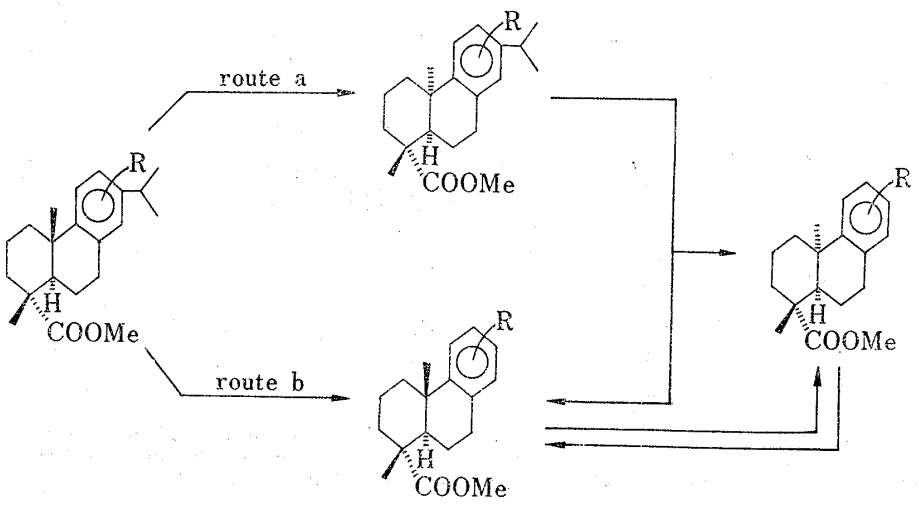


Chart 2

In conclusion, it can be stated that the reaction with aluminum chloride passes through the above courses (Chart II). At the first step, the isomerisation of 9,10-bond (route a) and deisopropylation (route b) proceed competitively and the course of the reaction is affected by the substituent in the aromatic ring. For instance, the reaction of 12-hydroxy ester (**7**)

proceeded through both routes (a and b) while 14-hydroxy ester (**19**) was selectively deisopropylated (route b). Accordingly, a possibility of the mechanism that isomerisation of 9,10-bond occurs simultaneously with deisopropylation should be excluded. In the last state of equilibrium, the reactant is all converted to *cis*- and *trans*-deisopropyl ester (*e.g.*, **10** and **9** from **7**) in predominance of the former isomer.

Experimental

All melting points were measured on the Kofler block and were uncorrected. NMR spectra were measured (δ) at 60 MHz in $CDCl_3$ *vs.* Me_4Si as internal reference. Infrared (IR) data (KBr disk) idicated maximum absorption in cm^{-1}. Gas-liquid chromatography (GLC) values were measured with a column condition (2 m×4 mm, 1.5% OV-17 on Shimalite W (80—100 mesh)).

Reaction of Methyl 12-Hydroxy-dehydroabietate (7) with Aluminum Chloride to 8, 9, and 10——A solution of 12-hydroxy ester[13] (**7**) (1.078 g) in ab. benzene (100 ml) was stirred with $AlCl_3$ (5.4 g, 12.43 mol. eq.) for 2 hr at room temperature. The reaction mixture was extracted with ether after H_2O was added and the extract was washed with 5% Na_2CO_3 aq., sat. NaCl aq., then was dried over Na_2SO_4. Removal of the solvent gave an oil (1.03 g), which was chromatographed on silica-gel (80 g) to be separated into four fractions by petr. ether–ether (4: 1) elution. The first fraction was the starting material (**7**) (90 mg, 8% yield). The second fraction (220 mg, 20% yield) was recrystallized from petr. ether to give colorless needles (**8**) (164 mg), mp 164—165.5°. *Anal.* Calcd. for $C_{21}H_{30}O_3$: C, 76.32; H, 9.15. Found: C, 76.00; H, 9.01. IR: 3420, 1705. NMR: 1.10 (s, 3H; 4-Me), 1.17 (s, 3H; 10-Me), 1.24 (d, 6H, J=7.2 Hz; iso-C_3H_7), 3.68 (s, 3H; COOMe), 4.97 (br. s, 1H; 12-OH), 6.65, 6.83 (s, 1H each; 11- and 14-H). The third fraction (354 mg, 38% yield) was recrystallized from ether–*n*-hexane to give colorless plates (**9**) (354 mg), mp 185—188°. *Anal.* Calcd. for $C_{18}H_{24}O_3$: C, 74.97; H, 8.39. Found: C, 74.64; H, 8.28. IR: 3420, 1697. NMR: 1.18 (s, 3H; 10-Me), 1.26 (s, 3H; 4-Me), 3.65 (s, 3H; COOMe), 5.08 (br. s, 1H; 12-OH), 6.47—6.97 (m, 3H; 11-, 13-, and 14-H). The fourth fraction (316 mg, 34% yield), IR: 3410, 1700. NMR: 1.08 (s, 3H; 4-Me), 1.16 (s, 3H; 10-Me), 3.72 (s, 3H; COOMe), 6.51—6.95 (m, 3H; 11-, 13-, and 14-H), was identical (IR and NMR) with the authentic sample[6] (**10**).

Methyl 10β-12-Hydroxy-13-deisopropyl-dehydroabietate (9) from Methyl Deisopropyl-dehydroabietate (12)——According to the synthetic method[8] of podocarpic acid type compound, the ester[14] (**9**) was obtained from methyl deisopropyl-dehydroabietate (**12**). The ester (**12**) (1 g) and acetyl chloride (2.53 g) in carbon disulfide (40 ml) were added slowly to aluminum chloride (4.33 g) and the mixture was stirred at room temperature for 24 hr. After H_2O was added, the reaction mixture was extracted with ether. The extract was washed with 5% Na_2CO_3 aq., sat. NaCl aq. and dried over Na_2SO_4. Removal of the solvent gave the oily product (1.085 g), which was chromatographed on basic alumina (80 g) by petr. ether–ether (4: 1) elution to give an oil (**13**). Mass: Calcd. for $C_{20}H_{26}O_3$: 314.1882. Found: 314.1866. IR (CCl_4): 1730, 1685, NMR: 1.17 (s, 3H; 10-Me), 1.25 (s, 3H; 4-Me), 2.49 (s, 3H; 12-COMe), 3.60 (s, 3H; 4-COOMe), 7.03 (d, 1H, J=8 Hz; 14-H), 7.60 (dd, 1H, J=8, 2 Hz; 13-H), 7.84 (d, 1H, J=2 Hz; 11-H). The acetyl ester (**13**) (502 mg) was oxidized in CH_2Cl_2 (3 ml) with AcO_2H (prepared from AcOH (1.8 g), conc. H_2SO_4 (0.02 ml), and 90% H_2O_2aq. (1.61 g)) at room temperature for 48 hr. After H_2O was added, the reaction mixture was extracted with ether and then, the extract was washed with sat. $NaHCO_3$aq., sat. NaCl aq. and dried over Na_2SO_4. Removal of the solvent gave an oily product (**14**) (384 mg). IR (CCl_4): 1765, 1730, 1205. The acetate (**14**) (384 mg) was hydrolyzed in conc. H_2SO_4 (1 drop)-H_2O (0.25 ml)-MeOH (50 ml) under reflux for 2 hr with stirring. The residue resulted by removal of MeOH, was extracted with ether and the extract was washed sat. $NaHCO_3$aq., sat. NaClaq. and dried over Na_2SO_4. The resulting oily product was recrystallized from ether–*n*-hexane to give colorless plates (**9**) (234 mg). The ester (**9**) was identical (IR and NMR) with the above-mentioned 10β-12-hydroxy-deisopropyl ester (**9**).

Methyl 10α-12-Methoxy-deisopropyldehydroabietate (16) from (10)——12-Hydroxy ester (**10**) (89 mg) was methylated (Me_2SO_4, K_2CO_3–acetone) as in the case of **22** to **21** and the resulting oil was purified by preparative thin-layer chromatography (silica-gel, petr. ether–ether (4: 1)). The solid was recrystallized from MeOH to give colorless plates (**16**) (37 mg), mp 103—104°. *Anal.* Calcd. for $C_{19}H_{26}O_3$: C, 75.46; H, 8.67. Found: C, 75.30; H, 8.41. IR: 1730. NMR: 1.05 (s, 3H; 4-Me), 1.18 (s, 3H; 10-Me), 3.65 (s, 3H; COOMe), 3.74 (s, 3H; OMe), 6.55—7.05 (m, 3H; 11-, 13-, and 14-H).

Reaction of Methyl 12-Methoxy-dehydroabietate (15) with Aluminum Chloride to 16, 17, and 18——12-Methoxy ester (**15**) (1.22 g) was reacted in ab. benzene (10 ml) with $AlCl_3$ (2.5 g, 5.30 mol. eq.) as in the case

13) R.C. Cambie and R.A. Franich, *Aust. J. Chem.*, **24**, 117 (1971).
14) The ester (**9**) was also obtained through the other route.[15] The NMR spectrum was identical with that of ours, but the melting point (138—142° and 149.5—151°) is different from ours (185—188°). They would be polymorphous.
15) T.A. Spencer, T.D. Weaver, R.M. Villarica, R.J. Friary, J. Posler, and M.A. Schwartz, *J. Org. Chem.*, **33**, 712 (1968).

of **7**. The resulting oily product was chromatographed on neut. alumina (100 g) to be separated into an oily product (**16**) (168 mg; 16% yield) by petr. ether–ether (9: 1) elution and an inseparable mixture (**15**, **17**, and **18**) (654 mg) by ether elution. The former part was recrystallized from MeOH to give colorless scales, mp 104—104.5°, which was identical with the authentic sample (**16**). The latter part was reacted with BBr_3 (2 ml) in CH_2Cl_2 (5 ml) under dry ice-acetone cooling for 10 min and then it was left standing at room temperature for 30 min. The reaction mixture was extracted with ether after ice-H_2O was added. The ether layer was extracted with 20% NaOHaq., the alkaline extract was acidified with conc. HClaq. and extracted with ether. The extract was washed with sat. NaClaq. and dried over Na_2SO_4. After the solution was methylated with CH_2N_2-ether solution, removal of the solvent gave a mixture (432 mg), which was chromatographed on silica-gel (50 g) to give four fraction by petr. ether–ether (4: 1) elution. The first fraction (30 mg, 3% yield) was identical (GLC) with **7**. The second fraction (79 mg, 7% yield) was recrystallized from petr. ether to give colorless prisms (53 mg), mp 160—162°, which were identical (mixed mp, IR, NMR, and GLC) with **8**. The third fraction (43 mg, 4% yield) was recrystallized from ether–*n*–hexane to give colorless plates (13 mg), mp 182.5—185.5°, which were identical (mixed mp, IR, NMR, and GLC) with **9**. The fourth fraction (25 mg, 2% yield) was identical (GLC) with **10**.

Methyl 14-Methoxy-dehydroabietate (20)——a) From 14-Amino-7-oxo Ester[10] (**23**) *via* 14-Methoxy-7-oxo Ester (**21**): 14-Amino-7-oxo-ester (**23**) (4.04 g) was treated in MeOH (850 ml)-conc. H_2SO_4 (43 ml) with $NaNO_2$ (1.22 g) under ice-cooling and the reaction mixture was stirred at room temperature for 2 hr. After urea (1.24 g) was added, the reaction mixture was treated as the usual manner. The resulting oil product (4.62 g) was chromatographed on silica-gel (200 g) to give two fractions. The first fraction (546 mg, 13% yield) was obtained from petr. ether–ether (19: 1) elution. It was recrystallized from MeOH to give pale yellow prisms (450 mg), which was identical (IR, NMR, and GLC) with **22**.[10] The second part (2.67 g, 63% yield) was obtained from petr. ether–ether (4: 1) elution. It was recrystallized from MeOH to give pale yellow prisms (**21**) (2.22 g), mp 98—100°. *Anal.* Calcd. for $C_{22}H_{30}O_4$: C, 73.71; H, 8.44. Found: C, 73.58; H, 8.09. IR: 1724, 1681. NMR: 1.16, 1.20 (d, 3H, J=7.2 Hz each; iso-C_3H_7), 1.20 (s, 3H; 10-Me), 1.34 (s, 3H; 4-Me), 3.65 (s, 3H; COOMe), 3.79 (s, 3H; 14-OMe), 7.06, 7.40 (d, 1H, J=8.4 Hz each; 11- and 12-H).

14-Hydroxy-7-oxo ester (**22**) (460 mg) was methylated with Me_2SO_4 (2 ml)-K_2CO_3 (2 g)-acetone (30 ml) under reflux for 24 hr. The filtrate of the reaction mixture was evaporated and extracted with ether after H_2O was added. The extract was washed with sat. NaClaq., dried over Na_2SO_4 and evaporated to give an oil (476 mg), which was chromatographed to give an oily product (236 mg, 49% yield). It was recrystallized from MeOH–H_2O to give pale yellow prisms (195 mg), which was identical (IR, NMR, and GLC) with **21**.

Under H_2-atmosphere (3 kg/cm^2), 14-methoxy-7-oxo ester (**21**) (300 mg) was hydrogenolyzed in AcOH (10 ml)-conc. H_2SO_4 (2 drops) with 10% Pd-C (200 mg). After the catalyst was filtered off, the filtrate was condensed, then diluted with H_2O and was extracted with ether. The extract was washed with sat. Na_2CO_3-aq., sat. NaClaq. and dried over Na_2SO_4. After the solvent was evaporated, the resulting oil (311 mg) was crystallized from MeOH to give colorless prisms (257 mg, 89% yield), mp 93—95°. *Anal.* Calcd. for $C_{22}H_{32}O_3$: C, 76.70; H, 9.36. Found: C, 77.00; H, 9.27. IR: 1730. NMR: 1.19 (s, 3H; 10-Me), 1.25 (s, 3H; 4-Me), 1.21 (d, 6H, J=7 Hz; iso-C_3H_7), 3.66 (s, 3H; COOMe), 3.69 (s, 3H; 14-OMe), 7.05 (s, 2H; 11- and 12-H).

b) From 14-Amino Ester[16] (**24**): **24** (329 mg) was treated in MeOH (75 ml)-conc. H_2SO_4 (3.75 ml) with $NaNO_2$ (207 mg) as in the case of **23** to **21**. The resulting oil (293 mg) was chromatographed on silica-gel (25 g) to give a fraction (171 mg, 50% yield) in petr. ether–ether (9: 1) elution. It was crystallized from MeOH to give colorless prisms (123 mg), mp 93—95°, which was identical (mixed mp, IR, NMR, and GLC) with **20**.

Methyl 14-Hydroxy-dehydroabietate (19)——a) From 14-Methoxy Ester (**20**): To a solution of 14-methoxy ester (**20**) (300 mg) in CH_2Cl_2 (3 ml), BBr_3 (1 ml)-CH_2Cl_2 (1 ml) was added under dry ice–acetone cooling. The mixture was treated as in the case of the work-up of the mixture (**15**, **16**, **17**, and **18**) into the corresponding hydroxy esters. The resulting oil (106 mg) was methylated (CH_2N_2–ether) and was purified by preparative thin-layer chromatography on silica gel (solvent: $CHCl_3$) to give colorless oil (**19**) (80 mg, 28% yield), bp 150° (bath temp.)/2×10^{-2} Torr. *Anal.* Calcd. for $C_{21}H_{30}O_3$: C, 76.32; H, 9.15. Found: C, 76.34; H, 9.21. IR (CCl_4): 3640, 1732. NMR: 1.23 (s, 3H; 10-Me), 1.31 (s, 3H; 4-Me), 1.25 (d, 6H, J=7.2 Hz; iso-C_3H_7), 3.69 (s, 3H; COOMe), 6.82, 7.05 (d, 1H, J=8.4 Hz each; 11- and 12-H).

b) From 14-Hydroxy-7-oxo ester (**22**): Under H_2-atomosphere (3 kg/cm^2), 14-hydroxy ester (**22**) (1.54 g) was hydrogenolyzed in AcOH (10 ml)-conc. H_2SO_4 (5 drops) with 10% Pd-C (500 mg). The reaction mixture was treated as in the case (**21**→**20**). The resulting oil (1.44 g) was chromatographed on silica-gel (50 g) to give oily product (**19**) (1.22 g; 82% yield) in petr. ether–ether (9: 1—4: 1) elution. The product was identical (IR, NMR, and GLC) with the sample (**19**) obtained by a)-method.

Reaction of Methyl 14-Hydroxy-dehydroabietate (19) with Aluminum Chloride to 25, and 26——14-Hydroxy ester (**19**) (537 mg) was reacted in ab. benzene (10 ml) with $AlCl_3$ (1.074 g, 4.96 mol. eq.) as in the case of **7**. The resulting oil (545 mg) was chromatographed on silica-gel (50 g) to give three fractions in petr. ether–ether (4: 1) elution, successively. The first fraction (136 mg; 29% yield) was recrystallized from petr. ether–benzene to give colorless prisms (35 mg), mp 154—157°, which was identical (mixed mp, IR, NMR, and GLC)

16) E. Ochiai and M. Ohta, *Yakugaku Zasshi*, **74**, 203 (1954).

with 10α-14-hydroxy ester [6](**26**). The second fraction (134 mg; 25% yield) was identical (GLC) with the starting material (**19**). The third fraction (192 mg; 41% yield) was recrystallized from MeOH to give colorless prisms (**25**) (174 mg), mp 147—149°. *Anal.* Calcd. for $C_{18}H_{24}O_3$: C, 74.97; H, 8.39. Found: C, 75.00; H, 8.24. IR: 3390, 1697. NMR: 1.19 (s, 3H; 10-Me), 1.27 (s, 3H; 4-Me), 3.66 (s, 3H; COOMe), 5.70 (s, 1H; 14-OH), 6.50—7.05 (m, 3H; 11-, 12-, and 13-H).

Reaction of Methyl 14-Methoxy-dehydroabietate (20) with Aluminum Chloride to 27, 28, and 34——14-Methoxy ester (**20**) (1.00 g) was reacted in ab. benzene (10 ml) with $AlCl_3$ (2 g, 5.17 mol. eq.) as in the case of **7**. The resulting product (1.014 g) was recrystallized from MeOH to colorless prisms (**27**) (331 mg, 33% yield), mp 172—172.5°. *Anal.* Calcd. for $C_{22}H_{32}O_3$: C, 76.70; H, 9.36. Found: 76.59; H, 9.16. IR: 1730. NMR: 1.12 (s, 3H; 4-Me), 1.21, (s, 3H; 10-Me), 1,21, 1.23 (d, 3H, J=7.2 Hz each; iso-C_3H_7), 3.69 (s, 3H; COOMe), 3.73 (s, 3H; 14-OMe), 7.06 (s, 2H; 11- and 12-H). After the mother liquor of the recrystallization was evaporated, the residue (669 mg) was treated in CH_2Cl_2 (9 ml) with BBr_3 (2 ml) in CH_2Cl_2 (3 ml) as in the case of the work-up of the mixture (**15**, **16**, **17**, and **18**) into the corresponding hydroxy esters. The resulting acidic part was methylated and then, the oily product (434 mg) was chromatographed on silica-gel (70 g) to give three fractions by petr. ether–ether (4: 1) elution, successively. The first fraction (88 mg; 11% yield) was recrystallized from petr. ether–benzene to give colorless prisms (54 mg), which was identical (mixed mp, IR, NMR, and GLC) with 10α-14-hydroxy-deisopropyl ester[6] (**26**). The second fraction (103 mg, 11% yield) was identical (GLC) with 10β-14-hydroxy ester (**19**). The third fraction (186 mg; 22% yield), was recrystallized from MeOH to give colorless prisms (86 mg), which was identical (mixed mp, IR, NMR, and GLC) with 10β-14-hydroxy-deisopropyl ester (**25**).

Methyl 10α-12-Methoxy-6,7-dioxo-deisopropyl-dehydroabietate (29)——12-Methoxy ester (**16**) (305 mg) in AcOH (21 ml) was oxidized with CrO_3 (420 mg) in 80% AcOHaq. (15 ml) as described in the reference.[4] The resulting yellow oil (257 mg) was purified by preparative thin-layer chromatography on silica-gel (petr. ether–ether (1: 1)) to give an oil (**29**) (78 mg). Mass. Calcd. for $C_{19}H_{22}O_5$: 330.1467. Found: 330.1468. IR (CCl_4): 1730, 1680. NMR: 0.74 (s, 3H; 4-Me), 1.28 (s, 3H; 10-Me), 3.33 (s, 1H; 5-H), 3.70 (s, 3H; COOMe), 3.94 (s, 3H; OMe), 6.88 (d, 1H, J=2.4 Hz; 11-H), 6.90 (dd, 1H, J=2.4, 9.6 Hz; 13-H), 8.09 (d, 1H, J=9.6 Hz; 14-H).

Methyl 10α-14-Methoxy-6,7-dioxo-dehydroabietate (30)——14-Methoxy ester (**27**) (400 mg) in AcOH (28 ml) was oxidized with CrO_3 (560 mg) in 80% AcOHaq. (20 ml) as in the case of **29**. The resulting oil (338 mg) was purified by preparative thin-layer chromatography on silica-gel (petr. ether–ether (1: 1)). The product separated was recrystallized from MeOH to give yellow needles (**30**) (97 mg), mp 160—164°. *Anal.* Calcd. for $C_{22}H_{28}O_5$: C, 70.94; H, 7.58. Found: C, 70.80; H, 7.03. IR: 1735, 1723, 1680. NMR: 0.66 (s, 3H; 4-Me), 1.22 (d, 6H, J=7.0 Hz; iso-C_3H_7), 1.26 (s, 3H; 10-Me), 3.24 (s, 1H; 5-H), 3.67 (s, 3H; COOMe), 3.72 (s, 3H; OMe), 7.13, 7.51 (d, 2H, J=8 Hz each; 11- and 12-H).

Methyl 10α-14-Hydroxy-dehydroabietate (33)——14-Methoxy ester (**27**) (222 mg) was demethylated (BBr_3) as in the case of the work-up the mixture (**15**, **16**, **17**, and **18**) into the corresponding hydroxy esters. The resulting product was methylated (CH_2N_2) to give crystalls (135 mg), which were recrystallized from petr. ether–ether to colorless prisms (94 mg), mp 154—155°. *Anal.* Calcd. for $C_{21}H_{30}O_3$: C, 76.32; H, 9.15. Found: C, 76.03; H, 8.89. IR: 3507, 1710. NMR: 1.13 (s, 3H; 4-Me), 1.21 (s, 3H; 10-Me), 1.26 (d, 6H, J=6.6 Hz; iso-C_3H_7), 3.70 (s, 3H; COOMe), 6.86, 7.06 (d, 1H, J=8.4 Hz each; 11- and 12-H).

Methyl 10α-12-Methoxy-dehydroabietate (17), Methyl 10β-12-Methoxy-deisopropyl-dehydroabietate (18), Methyl 10β-14-Methoxy-deisopropyl-dehydroabietate (34), and Methyl 10α-14-Methoxy-deisopropyl-dehydroabietate (28)——Hydroxy esters (**8**) (90 mg), (**9**) (200 mg), (**25**) (79 mg), and (**26**) (151 mg) were methylated (Me_2SO_4–K_2CO_3) as in the case of **22** to **21**. The products (**17**) (97 mg), Mass. Calcd. for $C_{22}H_{32}O_3$: 344.235. Found: 344.234. IR (CCl_4): 1725. NMR: 1.11 (s, 3H; 4-Me), 1.19 (d, 6H; J=7.2 Hz; iso-C_3H_7), 1.23(s, 3H; 10-Me), 3.70 (s, 3H; COOMe), 3.80 (s, 3H; OMe), 6.74, 6.87 (s, 1H, each; 11- and 14-H), (**18**) (201 mg), Mass. Calcd. for $C_{19}H_{26}O_3$: 302.188. Found: 302.188. IR (CCl_4): 1727. NMR: 1.20 (s, 3H; 10-Me), 1.27 (s, 3H; 4-Me), 3.65 (s, 3H; COOMe), 3.75 (s, 3H; OMe), 6.55—7.05 (m, 3H; 11-, 13-, and 14-H), (**34**) (80 mg), Mass. Calcd. for $C_{19}H_{26}O_3$: 302.188. Found: 302.191. IR (CCl_4): 1726. NMR: 1.23 (s, 3H; 10-Me), 1.29 (s, 3H; 4-Me), 3.69 (s, 3H; COOMe), 3.82 (s, 3H; OMe), 6.58—7.33 (m, 3H; 11-, 12-, and 13-H), and (**28**) (109 mg, purified by preparative thin-layer chromatography (petr. ether–ether; 4: 1)), Mass. Calcd. for $C_{19}H_{26}O_3$: 302.188. Found: 302.191. IR (CCl_4): 1725. NMR: 1.09 (s, 3H; 4-Me), 1.20 (s, 3H; 10-Me), 3.70 (s, 3H; COOMe), 3.83 (s, 3H; OMe), 6.56—7.31 (m, 3H; 11-, 12-, and 13-H), were obtained, respectively.