U.D.C. 547.677.3

13. **Michitoshi Ohta and Lara Ohmori**: Studies on Abietic Acid Derivatives. II. Deisopropylation of Dehydroabietic Acid. (2).

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It was shown in the preceding paper[1] that the oxidation of methyl deisopropyldehydroabietate (IIa) and its allo compound (IIb) with chromium trioxide afforded two kinds of isomers (IIIa and b) of 2,6-dimethyl-2-(*o*-carboxyphenyl)-6-methoxycarbonyl-1-cyclohexanone.

Treatment of (IIIa) and (IIIb) with 10% sodium hydroxide results in concurrent saponification of the ester and decarboxylation to respectively afford (IVa), m.p. 185~187°, $[\alpha]_D$ +142.5°, and (IVb), m.p. 185~187°, $[\alpha]_D$ −142.6°. In order to establish the purity of (IVb), its brucine salt was purified and the acid liberated but no change in the melting point or optical rotation was observed. It follows, therefore, that (IVb) is a unity. Thermal analyses of (IVa) and (IVb) indicated, as shown in Fig. 1, that they clearly formed a molecular compound of 1 : 1 ratio. Recrystallization of an equimolar mixture of (IVa) and (IVb) yields a racemic compound of m.p. 192~194°, $[\alpha]_D$ ±0° (cf. Fig. 2). The infrared spectra of (IVa) and (IVb) in carbon tetrachloride or Nujol are completely identical (cf. Fig. 3). These facts have definitely shown that (IVa) and (IVb) are antipodes. Since the infrared spectra of (IVa) and (IVb) exhibit the absorption of OH at 3.01 μ and of unsaturated, six-membered lactone ring at 5.91 μ, they are thought to form a lactol ring.[2]

Bromination of the two kinds of 9-oxo compound obtained in the earlier experiment,[1] i.e. methyl 9-oxodeisopropyldehydroabietate (Va) and its allo compound (Vb), in glacial acetic acid affords monobromo-ketones, (VIa), m.p. 133~134°, and (VIb), m.p. 121°. The two compounds, on boiling with silver nitrate in pyridine, respectively transits to unsaturated ketones, (VIIa), m.p. 105~106°, and (VIIb), m.p. 147~148°, by dehydrobromination. These ketones are vinilogs of β-ketocarboxylic esters and are decarboxylated on saponification with ethanolic potassium hydroxide, (VIIa) affording (VIIIa), m.p. 120~121°, $[\alpha]_D$ +106.3°, and (VIIb) affording (VIIIb), m.p. 120~121°, $[\alpha]_D$ −104.6°. The melting points of (VIIIa) and (VIIIb) are identical, the absolute values of specific optical rotation of the two are the same with reverse signs, and their infrared spectra in Nujol are completely identical, as shown in Fig. 3. It is certain therefore that they are antipodes.

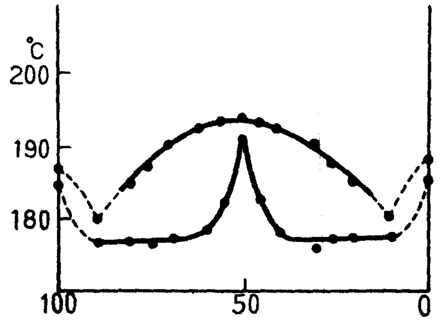

Fig. 1.

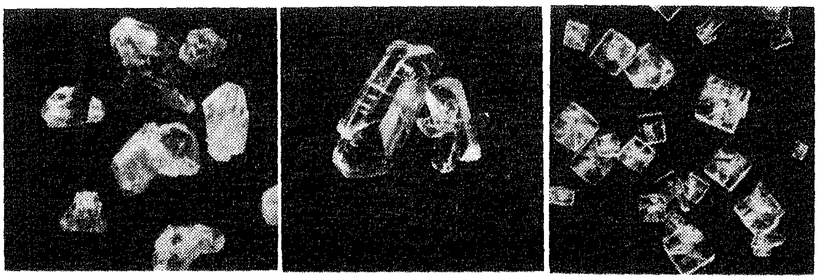
IVa IVb Racemate (IVa + IVb)

Fig. 2.

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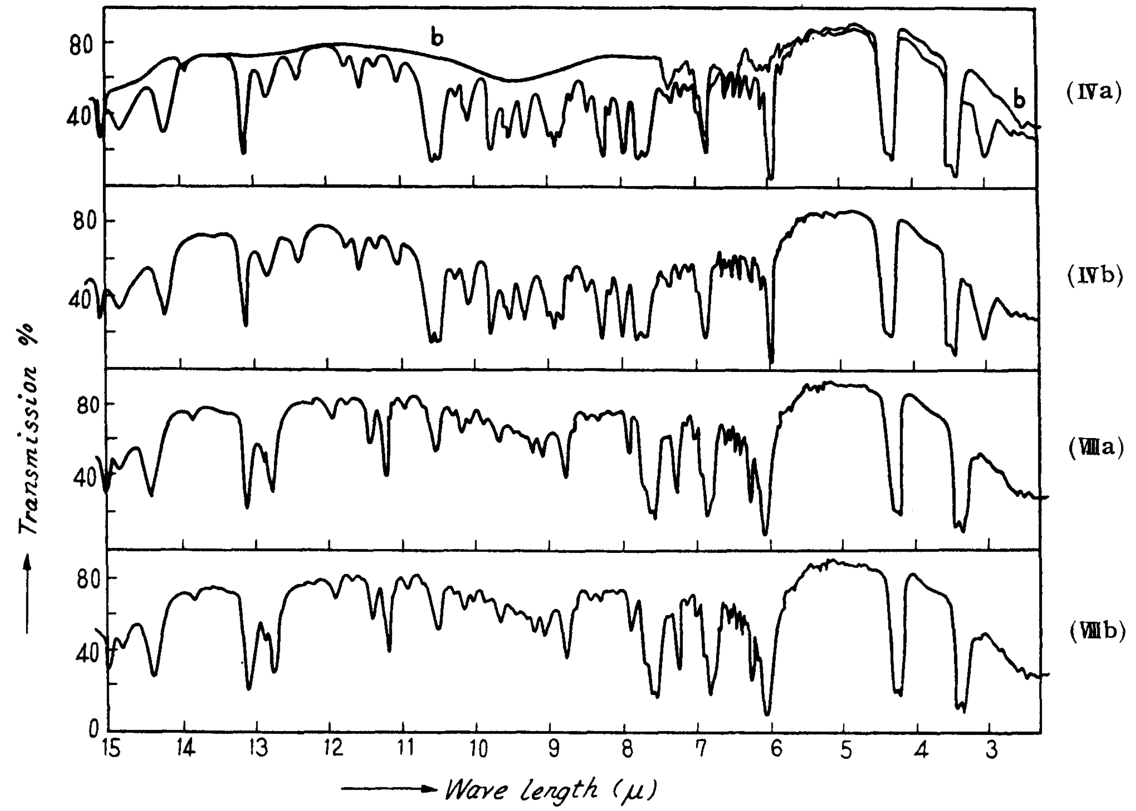
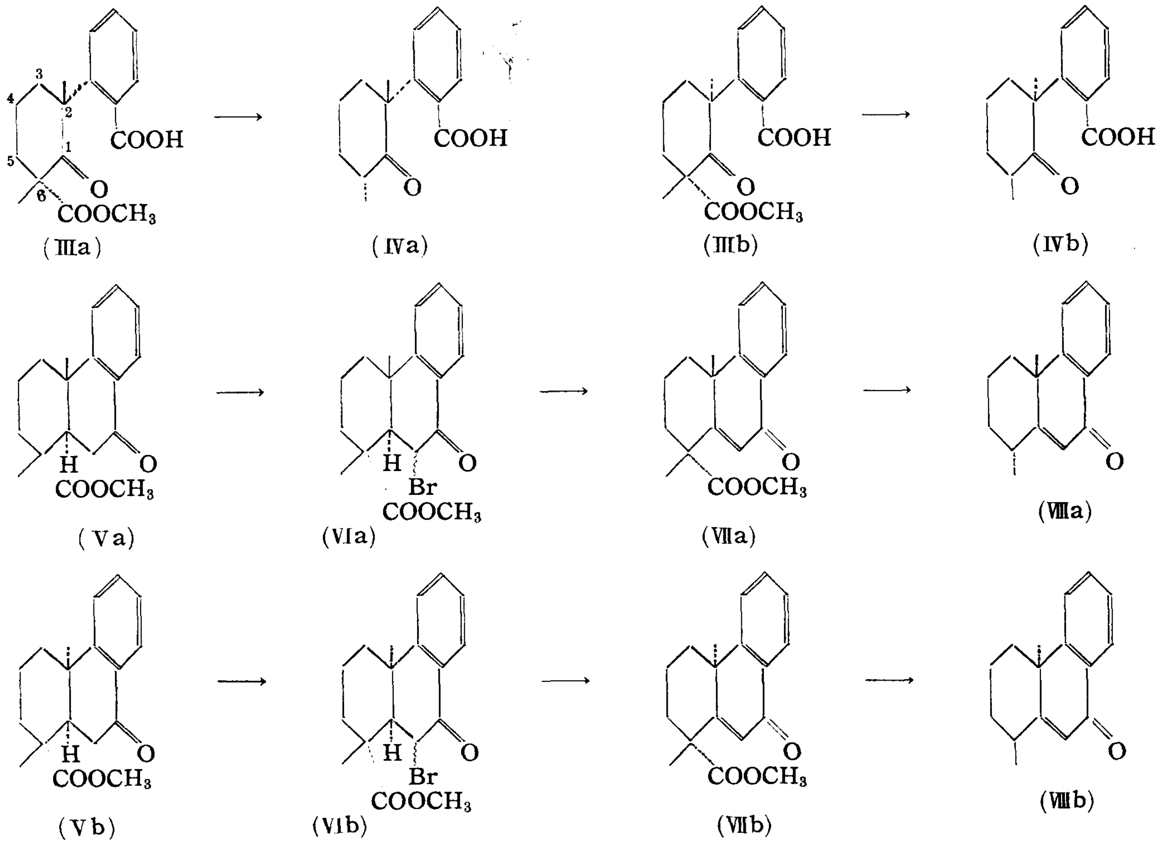
[1] Part I: This Bulletin, **5**, 91(1957).

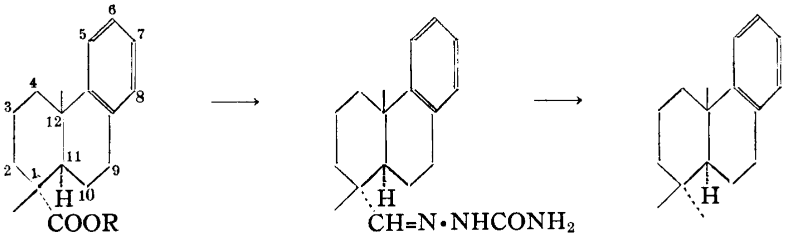
[2] H. A. Willis, *et. al.*: J. Chem. Soc., **1951**, 877; H. H. Zeiss, *et al.*: J. Am. Chem. Soc., **77**, 1643 (1955).



(Curve b : Back ground + Nujol)

Fig. 3.

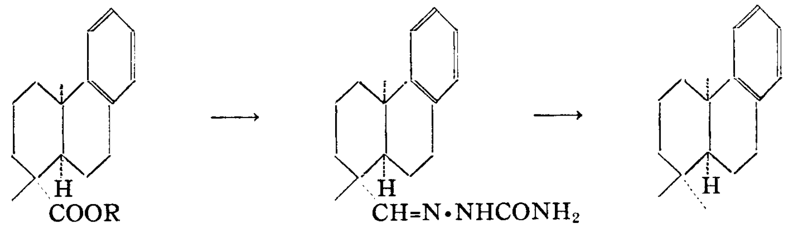




(Ia) R=H
(IIa) R=CH$_3$

(Xa)

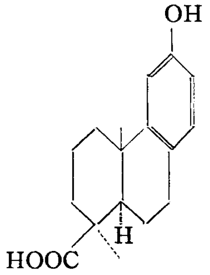
(XIa)



(Ib) R=H
(IIb) R=CH$_3$

(Xb)

(XIb)



(IX)

Comparison of the configurations of deisopropyldehydroabietic acid (Ia) and its allo compound (Ib) from the foregoing experiments clearly indicates that the C_{12}-methyl takes a reverse configuration in the two compounds, since (IVa) and (IVb), and (VIIIa) and (VIIIb), are mutual antipodes. The methyl in (Ia) is in β, as in dehydroabietic acid, so that the methyl in (Ib) would be in α. If the C_1-methyl in (Ib) is reverse of that in (Ia), (IIIa) and (IIIb), and (VIIa) and (VIIb), must be antipodes. Actually, however, they have different melting points and are not antipodes, so that the configuration at C_1 would be the same as in (Ia), the carboxyl being in α and the methyl in β. The fact that this methyl group takes reverse configurations in (IVa) and (IVb), and in (VIIIa) and (VIIIb), is thought to be due to the position of the methyl group being in the α-position (or its vinilog) of the ketone and easily takes the more stable equatorial position. Therefore, it is assumed that the C_1-methyl in (IVa) and (VIIIa) is in α and that in (IVb) and (VIIIb) is in β-position.

Finally, there is the configuration of C_{11}-position in (Ib). If C_{11} in (Ib) is in β-configuration, configurations at C_1, C_{11}, and C_{12} would be the reverse of podocarpic acid (IX) and the molecular rotation of (Ib) would naturally have the reverse sign and closely approximating absolute value of that of (IX) (M_D +366).[3] Actually, however, (Ib) has M_D +4, so that the C_{11} in (Ib) is in the same α-configuration as in (Ia). In order to clarify this point, the two compounds should be compared after being derived to the gem-dimethyl compounds by the reduction of carboxyl in (Ia) and (Ib).

(Ia) and (Ib) were derived to the respective acid chlorides with thionyl chloride and reduced by the Rosenmund process to the corresponding aldehydes. Without isolating the aldehydes, they were derived to the semicarbazones (Xa and b) and reduced by the Wolff-Kishner method, respectively affording deisopropyldehydroabietane (XIa), a liquid of $[\alpha]_D$ +65.0°, and deisopropylallodehydroabietane (XIb), crystals of m.p. 54°, $[\alpha]_D$ −28.2°. It cannot be believed that they are mutual antipodes and therefore, C_{11} in (Ib) retains the α-configuration as assumed and the A−B rings are in *cis*-bonding.

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3) L. F. Fieser, M. Fieser: "Natural Products Related to Phenanthrene," 3rd Ed., Reinhold Publishing Corp., 74(1949).

Experimental[4]

(+)-**2,6-Dimethyl-2-(*o*-carboxyphenyl)-1-cyclohexanone (IVa)**—A solution of 0.5 g. of (IIIa) dissolved in 5 cc. of 10% NaOH was heated at 100° for 2 hrs., cooled, acidified with HCl, and extracted with Et_2O. After drying over anhyd. Na_2SO_4, Et_2O was distilled off and the residue was recrystallized from MeOH to 0.3 g. of (IVa), m.p. 182~186°. Repeated recrystallizations raised the m.p. to 185~187°. *Anal.* Calcd. for $C_{15}H_{18}O_3$: C, 73.1; H, 7.4; neutr. equiv., 246. Found : C, 73.37; H, 7.78; neutr. equiv., 251. $[\alpha]_D^{25}$ +142.5°(c=2.204, EtOH). U.V. λ_{max}^{EtOH} mμ(log ε) : 238(3.96), 285(3.12). Infrared spectrum shown in Fig. 3.

(−)-**2,6-Dimethyl-2-(*o*-carboxyphenyl)-1-cyclohexanone (IVb)**—The same hydrolysis of 0.5 g. of (IIIb) and recrystallization from MeOH afforded 0.25 g. of (IVb), m.p. 183~186°. Several recrystallizations from MeOH raised the m.p. to 185~187°. *Anal.* Calcd. for $C_{15}H_{18}O_3$: C, 73.1; H, 7.4; neutr. equiv., 246. Found : C, 73.13; H, 7.39; neutr. equiv., 259. $[\alpha]_D^{23}$ −142.6°(c=1.388, EtOH). Infrared spectrum is shown in Fig. 3. Ultraviolet spectrum the same as that of (IVa).

Brucine salt of (IVb) : An equimolar mixture of (IVb) and brucine was recrystallized from MeOH, m.p. 157~160°.[5] *Anal.* Calcd. for $C_{38}H_{44}O_7N_2$: C, 71.2; H, 6.9; N, 4.4. Found : C, 71.70; H, 6.96. N, 4.76. $[\alpha]_D^{20}$ −101.3°(c=2.980, EtOH).

(±)-**2,6-Dimethyl-2-(*o*-carboxyphenyl)-1-cyclohexanone**—An equivalent mixture of (IVa) and (IVb) was recrystallized from MeOH, m.p. 192~194°; $[\alpha]_D^{22}$ ±0°(c=1.172, EtOH).

Methyl 9-Oxo-10-bromodeisopropyldehydroabietate (VIa)—A solution of 0.56 g. of Br_2 in 5 cc. of glacial AcOH was dropped into a stirred solution of 1 g. of (Va) dissolved in 5 cc. of glacial AcOH and added with 1 drop of glacial AcOH solution of HBr, while maintaining the solution at 35~40°. Glacial AcOH was distilled off under a reduced pressure and the residue was recrystallized from MeOH to 1.02 g.(80%) of (VIa), m.p. 131~133°. Further recrystallizations raised the m.p. to 133~134°. *Anal.* Calcd. for $C_{18}H_{21}O_3Br$: C, 59.2; H, 5.8. Found : C, 58.76; H, 5.80. $[\alpha]_D^{26}$ +21.9°(c=2.284, Me_2CO). U.V. λ_{max}^{EtOH} mμ(log ε) : 258(4.02), 293(3.34).

Methyl 9-Oxo-10-bromodeisopropylallodehydroabietate (VIb)—To a solution of 0.95 g. of (Vb) dissolved in 1 cc. of glacial AcOH and added with 0.47 cc. of 14% HBr-glacial AcOH solution, 5.55 cc. of 1*N* AcOH solution of Br_2 was added dropwise under stirring and the mixture was treated as in the foregoing section. Recrystallization from MeOH afforded 1.11 g. of crude (VIb), m.p. 106~114°. Further recrystallization raised the m.p. to 121°. *Anal.* Calcd. for $C_{18}H_{21}O_3Br$: C, 59.2; H, 5.8. Found : C, 59.15; H, 6.10. $[\alpha]_D^{25}$ −27.8°(c=1.580, Me_2CO), U.V. λ_{max}^{EtOH} 265 mμ (log ε 4.03).

Methyl 9-Oxo-$\Delta^{10(11)}$-deisopropyldehydroabietate (VIIa)—A mixture of 1.02 g. of (VIa) dissolved in 20 cc. of pyridine and 2 g. of $AgNO_3$ was boiled for 4 hrs., pyridine distilled off under a reduced pressure, dil. HCl was added to the residue, and extracted with Et_2O. After drying over anhyd. Na_2SO_4, Et_2O was evaporated and the residue was recrystallized from Et_2O-petr. ether to 0.4 g. of (VIIa), m.p. 105~106°. *Anal.* Calcd. for $C_{18}H_{20}O_3$: C, 76.0; H, 7.1. Found : C, 75.98; H, 7.21. $[\alpha]_D^{25}$ +85.6°(c=2.056, EtOH). U.V. λ_{max}^{EtOH} 255 mμ(log ε 4.13).

Methyl 9-Oxo-$\Delta^{10(11)}$-deisopropylallodehydroabietate (VIIb)—A mixture of 1.37 g. of (VIb) and 3.3 g. of $AgNO_3$ in 66 cc. of pyridine was boiled for 4 hrs. and treated as in the foregoing case, affording 0.43 g. of (VIIb), m.p. 147~148°. *Anal.* Calcd. for $C_{18}H_{20}O_3$: C, 76.0; H, 7.1. Found : C, 75.64; H, 7.25. $[\alpha]_D^{25}$ −154.4°(c=1.030, EtOH). U.V. λ_{max}^{EtOH} 255 mμ (log ε 4.20).

(+)-**1,12-Dimethyl-9-oxo-1,2,3,4,9,12-hexahydrophenanthrene (VIIIa)**—A mixture of 0.28 g. of (VIIa) and 5 cc. of 12% EtOH-KOH was boiled for 2 hrs., EtOH was distilled off under a reduced pressure, and the residue was extracted with Et_2O. After drying over anhyd. Na_2SO_4, Et_2O was evaporated and the residue was recrystallized from MeOH to 0.17 g. of (VIIIa), m.p. 120~121°. *Anal.* Calcd. for $C_{16}H_{18}O$: C, 84.9; H, 8.0. Found : C, 85.16; H, 8.15. $[\alpha]_D^{29}$ +106.3°(c=1.326, EtOH). U.V. λ_{max}^{EtOH} 255 mμ (log ε 4.22). I.R. λ_{max} 6.07, 6.25 μ (cf. Fig. 3).

(−)-**1,12-Dimethyl-9-oxo-1,2,3,4,9,12-hexahydrophenanthrene (VIIIb)**—The same hydrolysis as above of 0.35 g. of (VIIb) and recrystallization from MeOH afforded 0.1 g. of (VIIIb), m.p. 120~121°. *Anal.* Calcd. for $C_{16}H_{18}O$: C, 84.9; H, 8.0. Found : C, 84.84; H, 7.89. $[\alpha]_D^{29}$ −104.6°(c=1.214, EtOH). Ultraviolet and infrared spectra same as those of (VIIIa).

Deisopropyldehydroabietinal Semicarbazone (Xa)—A solution of 2.5 g. of (Ia) dissolved in 25 cc. of dehyd. Et_2O was added with 1.25 cc. of $SOCl_2$ and 1 drop of pyridine, and the mixture was allowed

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4) All m.p.s are uncorrected, optical rotation was measured in a 1-dm. tube, and infrared spectra were measured in Nujol with the Perkin-Elmer, single-beam spectrophotometer, Model 12C.

5) (IVb) regenerated from this brucine salt by treatment with AcOH melted at 185~187°, $[\alpha]_D^{20}$ −143.2° (c=2.200, EtOH).

to stand at room temperature for 5 hrs. This mixture was then washed with dil. Na_2CO_3 solution and water, dried over anhyd. Na_2SO_4, and Et_2O evaporated. The residue was recrystallized from petr. ether (with activated C) to 2.08 g. of a chloride, m.p. 82～85°.

This chloride was dissolved in 25 cc. of xylene, 0.5 g. of 10% Pd-$BaSO_4$ was added, and H_2 was bubbled through the mixture, while boiling under agitation. The reaction progressed about 85% in 50 mins. After cool, the catalyst was filtered off, xylene was evaporated, and the oily residue was dissolved in 10 cc. of. EtOH. Mixture of this solution and a solution of 1.5 g. of smicarbazide sulfate and 1.79 g. of AcONa dissolved in 4.5 cc. of water was boiled for 15 mins., worked up as usual, and recrystallized from dioxane to (Xa), m.p. 241°(decomp.). *Anal.* Calcd. for $C_{18}H_{25}ON_3$: C, 72.2; H, 8.4; N, 14.0. Found : C, 71.80; H, 8.26; N, 14.36.

Deisopropylallodehydroabietinal Semicarbazone (Xb)—One gram of (Ib) was treated as in the foregoing to the chloride, an oil (0.88 g.) of b.p$_{4.5}$ 176～177°, which was reduced similarly with 0.2 g. of 10% Pd-$BaSO_4$, and derived to the semicarbazone (Xb). Recrystallized from EtOH to crystals of m.p. 212°(decomp.). *Anal.* Calcd. for $C_{18}H_{25}ON_3$: C, 72.2; H, 8.4; N, 14.0. Found : C, 71.75; H, 8.32; N, 14.22.

Deisopropyldehydroabietane (XIa)—A mixture of 0.39 g. of (Xa) and EtONa (prepared from 0.33 g. of Na and 10 cc. of dehyd. EtOH) was placed in an autoclave and heated at 190～210° for 9 hrs. After evaporation of the solvent, water was added to the residue, and extracted with Et_2O. The Et_2O extract was dried over anhyd. Na_2SO_4, Et_2O distilled off, and the residue, dissolved in petr. ether, was passed through a column of 8 g. of alumina. The residue (0.15 g.) from the petr. ether eluate was distilled under a reduced pressure and afforded (XIa) as a fraction of b.p$_3$ 150～155°(bath temp.). *Anal.* Calcd. for $C_{17}H_{24}$: C, 89.4; H, 10.6. Found : C, 89.06; H, 10.44. $[\alpha]_D^{23}$ +65.0°(c=2.002, EtOH). U.V. λ_{max}^{EtOH} mμ (log ε) : 265(2.77), 273(2.74).

Further elution of the alumina column with Et_2O-petr. ether (1:1) afforded deisopropyldehydroabietinol, m.p. 62～64°.

Deisopropylallodehydroabietane (XIb)—Similar reduction of 0.38 g. of (Xb) afforded 0.24 g. of (XIb), b.p$_4$ 150～160°(bath temp.), which crystallized on standing and was recrystallized from MeOH to crystals of m.p. 53～54°. *Anal.* Calcd. for $C_{17}H_{24}$: C, 89.4; H, 10.6. Found : C, 89.47; H, 10.77. $[\alpha]_D^{22}$ −28.2°(c=1.100, EtOH). U.V. λ_{max}^{EtOH} mμ (log ε) : 267(2.80), 275(2.74).

Summary

It was established that deisopropylallodehydroabietic acid (Ib) had the methyl group between the two rings in α-configuration.

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