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Dehydroabietic Acid Derivatives. An Unusual α-Oxidation of a Ketone[1]

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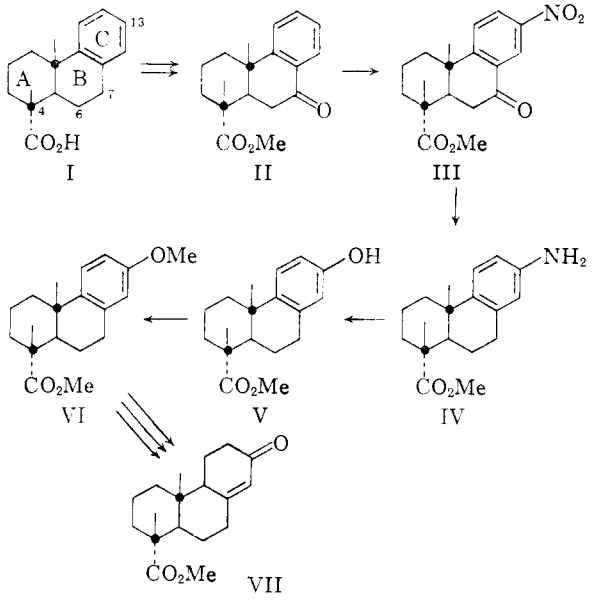
The conversion of deisopropyldehydroabietic acid into methyl 13-methoxydeisopropyldehydroabietate and the Birch reduction of the latter are discussed. The acid-catalyzed *t*-butyl hydroperoxide oxidation of methyl 7-ketodehydroabietate to the enol lactone of 6,7-diketodehydroabietic acid is described. The structure proof and the chemistry of this compound are presented.

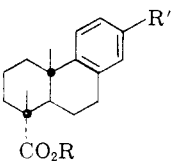
As part of our study of the total synthesis of diterpenic substances[2] it became necessary to convert deisopropyldehydroabietic acid (I) into the hydroaromatic system VII. This transformation has been performed by the route illustrated in Chart I.

CHART I

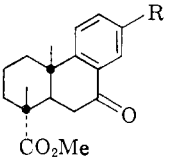


d-Deisopropyldehydroabietic acid (I) has been prepared by a multistage oxidative deisopropylation of dehydroabietic acid (VIIIa)[3] as well as by a one-step aluminum chloride-induced dealkylation of the same acid[3] or its derivative.[4] Methylation and chromic acid oxidation of *d*-deisopropyldehydroabietic acid (I) has been reported to yield II among other oxidation products.[3] Oxidation of the methyl ester of I under the milder conditions which were reported for the conversion of the nitrile of I into its 7-keto derivative[4] has led now to II as the exclusive product.

Nitration[5] of the ketoester II gave the 13-nitro compound III, whose catalytic hydrogenation afforded the aminoester IV. Diazotization of IV and acid-catalyzed hydrolysis led to the phenolic ester V, which could be converted to VI on treatment with dimethyl sulfate and alkali. Reduction of compound VI with lithium and alcohol in liquid ammonia and acid treatment of the dihydro product yielded a conjugated ketone carbinol, which, without purification, was oxidized with chromic acid and methylated with diazomethane. These three operations gave crystalline enone ester VII.



VIIIa, R = H, R' = *i*-Pro
b, R = Me, R' = CO_2H



IXa, R = CO_2H
b, R = OH
c, R = $C(CH_3)=CH_2$
d, R = *i*-Pro

Several of the compounds in Chart I could be prepared also by other means, their identity checked and their supply increased. Thus the aminoester IV proved to be identical with the last intermediate in Ohta's oxidative degradation of dehydroabietic acid (VIIIa) to its deisopropyl derivative I.[3] In this degradation scheme three steps had been expended on the conversion of the ketoester acid IXa to its desoxy derivative VIIIb (Wolff–Kishner reduction, esterification and partial saponification). Catalytic hydrogenation now accomplished the same task in one step.[6]

The phenolic ester V proved to be identical with the product of catalytic hydrogenation of the ketophenol IXb. The latter had been prepared previously by another oxidative degradation of dehydroabietic acid (VIIIa).[7] The unsaturated ketoester VII was identical with the product of partial ozonolysis of methyl neoabietate.[8] Since the introduction of asymmetry into C-9 in the hydrolytic work-up of the product of Birch reduction must lead to the thermodynamically more favorable C(9)-H α-configuration and since the ozonolytic production of VII could not have affected the C-9 asymmetry, the identity of products proves the presence of this C-9 configuration in neoabietic acid (X). This constitutes the first chemical proof of the C-9 stereochemistry of this resin acid.[9]

An Unusual α-Oxidation.—As part of the above synthesis the Sanderson *t*-butyl hydroperoxide oxidation of the olefinic ketoester IXc to the keto-

(1) The authors are indebted to the National Science Foundation and to Ciba Pharmaceutical Products, Inc., for financial support of this work.

(2) *Cf.* E. Wenkert and A. Tahara, *J. Am. Chem. Soc.*, **82**, 3229 (1960).

(3) M. Ohta and L. Ohmori, *Pharm. Bull. Tokyo*, **5**, 91, 96 (1957), and references contained therein.

(4) E. Wenkert and J. W. Chamberlin, *J. Am. Chem. Soc.*, **81**, 688 (1959).

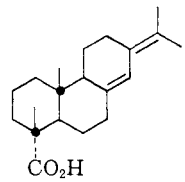
(5) *Cf.* R. Hodges and R. A. Raphael, *J. Chem. Soc.*, 50 (1960).

(6) This experiment was performed by Mr. Virgil I. Stenberg.

(7) (a) P. F. Ritchie, T. F. Sanderson and L. F. McBurney, *J. Am. Chem. Soc.*, **76**, 723 (1954); (b) T. F. Sanderson (to Hercules Powder Co.), U. S. Patents 2,750,367 and 2,750,368.

(8) *Cf.* G. C. Harris and T. F. Sanderson, *J. Am. Chem. Soc.*, **70**, 339 (1948); W. M. Hoehn (to G. D. Searle & Co.), U. S. Patent 2,682,555.

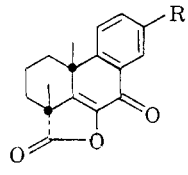
(9) For a physical proof *cf.* C. Djerassi, R. Riniker and B. Riniker, *J. Am. Chem. Soc.*, **78**, 6362 (1956).



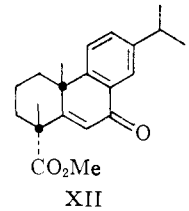
X

phenol IXb[7b] had to be repeated. In order to increase yields of the desired product, the effect of increasing concentration of the oxidizing agent on the course of the reaction was investigated, and led to the formation of an unexpected $C_{17}H_{16}O_4$ lactone. Since the creation of a lactone implied the participation of the 4α-carbomethoxy group in the reaction, and since such lactone in an A/B *trans* ring system could not be bridged beyond C-6, the oxidation appeared to have taken place α to the 7-keto group. The lack of precedence of such *t*-butyl hydroperoxide-induced α-oxidations suggested a study of the reaction with a less complex substrate, methyl 7-ketodehydroabietate (IXd).[7a,10]

Exposure of IXd to *t*-butyl hydroperoxide and a trace of concentrated sulfuric acid in acetic acid for 55 hours at 50–55° produced a ketolactone in high yield. Similar results were obtained with the use of di-*t*-butyl peroxide or *t*-butyl peracetate, but not with 30% hydrogen peroxide. On the basis of its physical properties and elemental analysis the lactone seemed to be the compound most recently reported to be the product of the selenium dioxide oxidation of methyl 7-ketodehydroabietate (IXd) and for which XIa has been suggested as structural formula.[11] Repetition of the latter oxidation led in our hands mostly to the unsaturated ketoester XII but also to some of the ketolactone. Direct comparison of the lactones from the two different oxidations unambiguously proved their identity.

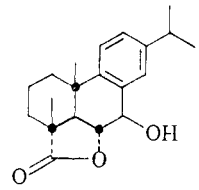


XIa, R = *i*-Pro
d, R = OH

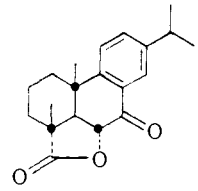


XII

Whereas previous[11] results, our spectral data and the elemental analysis of the ketolactone were in agreement with the proposed structure XIa, insufficient information was available for the structure to be considered fully established. Catalytic hydrogenation of the lactone yielded dehydroabietic acid (VIIIa), indicating that no skeletal rearrangement had taken place in the formation of the lactone. Selenium dioxide oxidation left the lactone unchanged, a result compatible with structure XIa. Sodium borohydride reduction led to a hydroxylactone, whose oxidation with chromic acid yielded a ketolactone different from XIa but readily convertible into the latter by selenium dioxide oxidation. This reaction cycle furnished unambiguous proof of structure XIa for the original ketolactone. It also revealed a rare example of an exhaustive borohydride reduction of an α,β-unsaturated ketone to a saturated alcohol.[12] While the stereochemistry of the latter at C-5, -6 and -7 was not ascertained, it is most likely that depicted in XIII, on the assumption that stereospecific hydride attack had taken place at C-5 from the α-side of XIa, thermodynamically controlled protonation at C-6 of the resulting enolate ion had followed leading to a *cis*-locked lactone, and that the remaining 7-keto group had been reduced specifically from its α-side also.[13] If this stereochemistry is accepted for XIII, the configuration of its oxidation product must be that shown in XIV. The infrared absorption of the latter's lactone carbonyl group was strikingly anomalous. While the hydroxylactone XIII revealed a normal 5.66 μ γ-lactone peak and the low wave length 5.53 μ lactone absorption of XIa was expected for an enol γ-lactone, especially one δ-substituted by a ketone group, a 5.51 μ lactone peak was most unusual for the saturated ketolactone XIV. The coplanar configuration of the rigidly held, equatorial lactone group and the 7-keto function may be responsible for this strong shift of the lactone carbonyl absorption to lower wave length.[14]



XIII



XIV

During a search for alternative synthetic routes toward ketolactone XIV, methyl 7-ketodehydroabietate (IXd) was brominated and the resulting 6-bromo derivative exposed to solvolysis. Collidine treatment of the latter, in a manner in which a 6-bromo-7-ketopodocarpic acid derivative has been reported to have been converted into an axial lactone analog of XIV,[15] yielded only the elimination product XII. Dimethyl sulfoxide treatment of the 6-bromo compound afforded only the enol-lactone XIa. This exceedingly slow transformation (a 50% yield of product in 10 days) must have involved an actual dimethyl sulfoxide displacement of the bromide, disproportionation of the resulting salt into dimethyl sulfide and a 6,7-diketone,[16] the latter's enolization and spontaneous cyclization of the mono-enol into the lactone XIa.

(10) E. Wenkert and B. G. Jackson, *J. Am. Chem. Soc.*, **80**, 211 (1958).

(11) R. Dulou and G. Defaye-Duchateau, *Compt. rend.*, **250**, 1288 (1960).

(12) For citation of a few analogies *cf.* W. J. Gensler, F. Johnson and A. D. B. Sloan, *J. Am. Chem. Soc.*, **82**, 6074 (1960) and references therein.

(13) The possibility of the reduction having taken the course of prior hydrolysis of the enol lactone XIa, borohydride reduction of the resulting (possibly 5-epimeric) 6,7-diketo acid, and relactonization on work-up cannot be excluded. As a consequence the stereochemical assignment of C-5 and -7 in XIII and of C-5 in XIV must be considered as only tentative at this time.

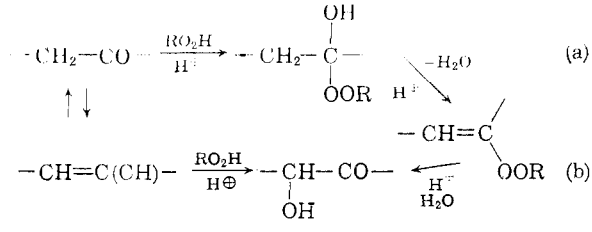
(14) A very similar case involving an axial lactone substituent appears not to exhibit this shift (E. Wenkert and C. D. Roth, unpublished observation).

(15) R. H. Bible, Jr. (to G. D. Searle and Co.), U. S. Patent 2,753,357.

(16) *Cf.* N. Kornblum, J. W. Powers, G. J. Anderson, W. J. Jones, H. O. Larson, O. Levand and W. M. Weaver, *J. Am. Chem. Soc.*, **79**, 6562 (1957).

In view of the assignment of structure XIa to the product of the *t*-butyl hydroperoxide oxidation of methyl 7-ketodehydroabietate (IXd), it is possible now to designate XIb as the phenolic product of the over-oxidation of the olefinic ketoester IXc by *t*-butyl hydroperoxide. Such conversions of an α-ketomethylene group to the state of oxidation of a carbonyl function appear to be unprecedented. In the two cases under consideration two oxidative steps and a lactonization seem to have occurred. The following evidence indicated that the lactonization took place after the oxidations. *t*-Butyl hydroperoxide oxidation of the ketolactone XIV yielded no enol-lactone XIa but only a mixture whose infrared absorption in the carbonyl region (no peaks above 5.7 μ) revealed a change of the functionality of the starting material at the site of its aromatic keto group. Furthermore, the fact that a 6,7-diketoester readily enolizes and lactonizes into XI was shown firstly by the dimethyl sulfoxide experiment (*vide supra*) and secondly by the observation that acidification of the yellow aqueous alkaline solution obtained by the instantaneous hydrolysis of an otherwise colorless water-insoluble lactone XIa to a 6,7-diketoacid led back to the lactone XIa.

The unusual peroxide-induced α-oxidation is open to two formal mechanistic interpretations. One, path a, suggests that the peroxide undergoes an acid-catalyzed addition to the ketone, followed by a similarly catalyzed dehydration, and that the resulting alkenyl peroxide is transformed to an α-ketol through nucleophilic attack by the solvent in a manner similar to the oxidations of ketones by selenium dioxide or chromic acid.[10,17] This route is open to two objections. Firstly, the initial addition intermediate is equivalent with one postulated for the Baeyer–Villiger oxidation of ketones[18] and thus would be expected to disproportionate into *t*-butyl alcohol and a lactone. Secondly, the final solvent attack could lead to an α-ketol, and to an α-diketone at a later stage, only in the presence of a fair concentration of water, a condition not satisfied by the experiments under consideration. Hence an alternate route, path b, appears more plausible. It involves prior enolization of the ketone and electrophilic attack of the conjugate acid of *t*-butyl hydroperoxide on the enol in a manner analogous to the well-known route of halogenation of ketones. An oxidation of the resultant α-ketol would lead to an α-diketone, which in the above diterpene cases constitutes the crucial immediate precursor of the lactones XIII.



(17) *Cf.* E. J. Corey and J. P. Schaefer, *J. Am. Chem. Soc.*, **82**, 918 (1960).

(18) *Cf.* C. H. Hassall, Chapter 3 in "Organic Reactions," Vol. IX, John Wiley and Sons, Inc., New York, N. Y., 1957.

Experimental

Methyl 7-Ketodeisopropyldehydroabietate (II).—Diazomethane treatment of *d*-deisopropyldehydroabietic acid (I)[3,4] gave its methyl ester,[3] 75 mg. of which was oxidized with chromic acid according to a previous procedure.[10] Alumina chromatography and petroleum ether elution yielded 14 mg. of starting ester, m.p. 106–108° after crystallization from methanol. Elution with 9:1 petroleum ether–ether gave 50 mg. of a solid product, m.p. 43–48°. Crystallization of the latter from petroleum ether yielded white prisms of methyl 7-ketodeisopropyldehydroabietate (II), m.p. 50–51° (lit.[3] m.p. 50–51°); $[\alpha]_D$ +6.7° (MeOH) (lit.[3] +6.7°); infrared spectrum ($CHCl_3$), C=O 5.74(s), 5.89(s)μ.

Anal. Calcd. for $C_{18}H_{22}O_3$: C, 75.49; H, 7.74. Found: C, 75.53; H, 7.63.

Methyl 7-Keto-13-nitrodeisopropyldehydroabietate (III).—The ketoester II, 24 mg., was added to a solution of 0.02 ml. of concd. nitric acid and 0.1 ml. of concd. sulfuric acid at 0°. After the mixture had been stirred for 10 minutes at 0°, it was poured on ice. The resulting precipitate was filtered and the filtrate extracted with ether. The extract was washed with water, dried over sodium sulfate and evaporated. The combined residue and aforementioned precipitate, 25.5 mg., were crystallized from methanol yielding 18 mg. of white needles of the desired nitration product III, m.p. 152–154°, $[\alpha]_D$ +38.9° (MeOH).

Anal. Calcd. for $C_{18}H_{21}O_5N$: C, 65.24; H, 6.39; N, 4.23. Found: C, 65.69; H, 6.40; N, 4.53.

Methyl 13-Aminodeisopropyldehydroabietate(IV).—A mixture of 11 mg. of III, 10 mg. of palladium–charcoal, 5 mg. of palladium chloride and 5 drops of concd. hydrochloric acid in 10 ml. of ethanol was hydrogenated at room temperature and atmospheric pressure for 5 hr. The catalyst was filtered, the solution evaporated, 10% sodium carbonate solution added to the residue and the aqueous solution extracted with ether. The extract was washed with saturated brine solution, dried over sodium sulfate and evaporated. The oily residue, 6 mg., was chromatographed on deactivated alumina. Benzene elution yielded 1.5 mg. of a product which gave white needles of desired amine IV on crystallization from benzene–petroleum ether. Its m.p., m.m.p. 102–104°(lit.[3] m.p. 104–105°) and infrared spectrum were identical with those of an authentic sample obtained by Ohta's method.[3] Crystallization of the amine hydrochloride from water gave long white needles, m.p. 185–190°.

One of the modifications of the Ohta synthesis of amine IV involved the one-step reduction of methyl 7-keto-13-carboxydeisopropyldehydroabietate (IXa) to methyl 13-carboxydeisopropyldehydroabietate (VIIIa). A mixture of 50 mg. of IXa, m.p. 200–208°(lit.[3] m.p. 195–200°), and 50 mg. of palladium–charcoal in 5 ml. of ethyl acetate was hydrogenated at room temperature and atmospheric pressure for 22 hr. The catalyst was filtered and the solution evaporated leaving 45 mg. of crystals, m.p. 176–179°. Crystallization from aqueous methanol produced crystalline acid VIIIa, m.p. 180–182°(lit.[3] m.p. 179–181°).

Methyl 13-Hydroxydeisopropyldehydroabietate (V).—A solution of 50 mg. of sodium nitrite in 1 ml. of water was added dropwise to an ice-cold stirring suspension of 90 mg. of amino ester IV in 4 ml. of 10% hydrochloric acid. After 20 min., 80 mg. of urea was added to the suspension. After 10 more min. the precipitate was filtered and washed with cold water. The combined filtrates were poured into a solution of 20 ml. of 15% sulfuric acid, heated at 80° for 20 min. and kept standing for 12 hr. The mixture was extracted with ether. The extract was washed with saturated brine solution, dried over anhydrous sodium sulfate and evaporated. The solid, 83 mg., was crystallized four times from aqueous methanol affording colorless crystals of the phenol ester V, m.p. 147.5–148.5°, $[\alpha]_D$ + 55.3°; ultraviolet spectrum (95% ethanol) λ_{max} 279 mμ (log ϵ 3.32) and 285 mμ (log ϵ 3.28).

Anal. Calcd. for $C_{18}H_{24}O_3$: C, 74.97; H, 8.39. Found: C, 74.75; H, 8.39.

Methyl 13-Methoxydeisopropyldehydroabietate (VI).—A mixture of 100 mg. of the phenol ester V, 0.15 ml. of dimethyl sulfate and 500 mg. of potassium carbonate in 10 ml. of acetone was heated on a water-bath under nitrogen for 15 hr. and then was left standing at room temperature for 12 hr. After vacuum removal of acetone the mixture was dissolved in ether, washed with 4% sodium hydroxide solution

and with water and dried over anhydrous sodium sulfate. Evaporation of the solvent left 100 mg. of crystals which on crystallization from methanol gave 93 mg. of colorless prisms of the methyl ether ester VI, m.p. 79.5°–80.5°, $[\alpha]_D$ +32.8°; ultraviolet spectrum (95% ethanol) λ_{max} 277 mμ (log ε 3.34) and 284 mμ (log ε 3.31).

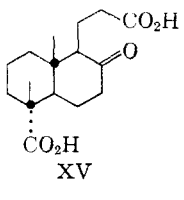
Anal. Calcd. for $C_{19}H_{26}O_3$: C, 75.46; H, 8.66. Found: C, 75.29; H, 8.76.

Ketoester VII. (a).—Over a period of 20 min., 800 mg. of finely divided lithium strips, 6 ml. of absolute ethanol and 5 ml. of liquid ammonia were added to a stirring solution of 50 mg. of ester VI in 1.5 ml. of dry ether and 5 ml. of absolute ethanol. The henna lithium layer disappeared after 40 minutes, whereupon the mixture was left standing for 12 hr. Ether and water were added, the ether extract washed with saturated brine solution and evaporated. A solution of the residue, 37 mg., and 1 ml. of concd. hydrochloric acid in 2.5 ml. of water and 13 ml. of ethanol was heated at 80–90° under a nitrogen atmosphere for 90 min. The solution was diluted with water and extracted with ether. The extract was washed with brine solution, dried over anhydrous sodium sulfate and evaporated. A solution of the residual oil, 32 mg., in 2.5 ml. of a 0.9% (by weight) chromic acid–acetic acid solution was left standing with occasional shaking at room temperature for 2 hr. The solvent was removed in vacuum, water was added and the solution extracted with ether. The extract was washed with water, 2 *N* sodium carbonate solution and again with water, dried and evaporated. The remaining oil, 21 mg., seemed to be a ketoaldehyde (VII, CHO in place of CO_2-Me); infrared spectrum ($CHCl_3$), CH3.75(m)μ, C=O 5.80(s), 6.00(s)μ. Reoxidation of the latter by the same chromic acid procedure, acidification of its and the previous sodium carbonate extracts with hydrochloric acid, extraction of the combined acid solutions with ether and evaporation of the organic extracts led to 22 mg. of an acid, presumably VII (CO_2H in place of CO_2Me); infrared spectrum ($CHCl_3$): OH 2.85(w), 3.20–3.30(m)μ; C=O 5.87(s), 6.00(s)μ; C=C 6.20(m)μ.

An ethereal solution of 41.5 mg. of ketoacid was treated with an ether solution of diazomethane for 12 hr. The solution was washed with 5% sodium carbonate solution and water, dried and evaporated. The residue, 40 mg., was chromatographed on 16 g. of deactivated alumina. Elution with benzene yielded 21 mg. of white solid which on crystallization from methanol gave 16 mg. of colorless prisms of ketoester VII, m.p., m.m.p. 127–128°, $[\alpha]_D$ +36.2°(MeOH); infrared spectrum (KBr) identical with that obtained by the ozonolysis of methyl neoabietate (*vide infra*).

(b).—Ozone was passed through a solution of 400 mg. of neoabietic acid[19] in 20 ml. of freshly distilled methylene chloride at −70° for 2.5 min. Then oxygen was passed through the solution to expel the excess ozone. The solution was added dropwise to 50 ml. of hot water, the mixture heated on a steam-bath for 2 hr. and finally extracted three times with 30-ml. portions of ether. The combined extracts were dried over sodium sulfate and evaporated. After some standing, the residue, triturated with a mixture of ether and petroleum ether, solidified. Two crystallizations from ethyl acetate gave 55 mg. of colorless crystals, m.p. 214–217°. Recrystallization yielded colorless prisms of the diacid XV, m.p. 218.5–220°, $[\alpha]_D$ −10.4° (MeOH); infrared spectrum ($CHCl_3$), OH 2.8–3.3(w) μ, C=O 5.85(s) μ.

Anal. Calcd. for $C_{16}H_{24}O_5$: C, 64.84; H, 8.16. Found: C, 64.84; H, 8.21.



XV

Identical ozonolysis of 270 mg. of methyl neoabietate, prepared by a standard diazomethane treatment of neoabietic acid, yielded an ether solution which was washed with 30 ml. of 5% potassium carbonate solution and 10 ml. of saturated brine solution and dried over sodium sulfate. Evaporation of the solvent left 226 mg. of a neutral oil whose chromatography on silica and elution with 9:1 benzene–ether gave 70 mg. of a solid. Two crystallizations from petroleum ether yielded 59 mg. of colorless crystalline ketoester VII, m.p. 127–128° (lit.[8] m.p. 127–128°), $[\alpha]_D$ +38.3° (MeOH) (lit.[19] $[\alpha]_D$ +32° in dioxane).

Anal. Calcd. for $C_{18}H_{26}O_3$: C, 74.44; H, 9.03. Found: C, 74.57; H, 9.23.

Acidification of the potassium carbonate washings and ether extraction gave 27 mg. of acidic product. A mixture of 123 mg. of this acid product and 200 mg. of potassium hydroxide in 6 ml. of ethylene glycol and 0.9 ml. of water was refluxed for 8 hr. under nitrogen. Acidification of the mixture with dilute hydrochloric acid, extraction with ether and evaporation yielded 92 mg. of residue whose chromatography on silica and elution with 3:1 benzene–ether led to 54 mg. of an oil. After standing a long time in ethyl acetate and being seeded with a crystal of authentic XV, 10 mg. of crystals deposited. Crystallization from ethyl acetate yielded colorless prisms of the keto diacid XV, m.p., m.m.p. 218–219.5°.

Oxidations of IXc.—A mixture of 800 mg. of IXc, 0.6 ml. of *t*-butyl hydroperoxide and 6 drops of concd. sulfuric acid in 10 ml. of acetic acid was kept at 33° for 7 hr. and at room temperature for another 12 hr. The mixture was diluted with water and extracted with ether. The extract was washed with sodium bicarbonate solution, extracted with 5% sodium hydroxide solution, washed with water, dried over anhydrous sodium sulfate and evaporated. Chromatography of the oily residue, 433 mg., on alumina and elution with 2:1 benzene–ether gave 80 mg. of solid. Three crystallizations from methanol yielded methyl 7-keto-13-acetyldeisopropyldehydroabietate (IX, R = Ac), m.p., m.m.p. 144–146° (lit.[7] m.p. 144–146°), infrared spectrum identical with that of an authentic sample.[7]

The sodium hydroxide extract was acidified and extracted with ether. The extract was dried over magnesium sulfate, evaporated and the residue, 398 mg., triturated with methanol. Crystallization of the resulting solid from aqueous methanol led to 289 mg. of crystals, m.p. 172–180°, which on further crystallizations became pure methyl 7-keto-13-hydroxydeisopropyldehydroabietate (IXb), m.p., m.m.p. 196–197° (lit.[7] m.p. 196–197°), infrared spectrum identical with that of an authentic specimen.[7]

An increase up to a 20 mole excess of the *t*-butyl hydroperoxide used and/or keeping the reaction mixture at 40° for 24 hr. resulted in the conversion of IXc into 5(6)-dehydro-6,13-dihydroxy-7-ketodeisopropyldehydroabietic lactone (XIb), m.p. 240–242° after crystallization from methanol, $[\alpha]_D$ −29.0° ($CHCl_3$); spectra: ultraviolet (95% ethanol), λ_{max} 222 mμ (log ε 4.28), 265 mμ (log ε 3.99) and 289 mμ (log ε 4.00); infrared ($CHCl_3$), OH 2.83(w), 3.08(m) μ; C=O 5.53(s), 6.00(s), 6.06(s) μ; C=C 6.23(m) μ.

Anal. Calcd. for $C_{17}H_{16}O_4$: C, 71.82; H, 5.67. Found: C, 72.46; H, 6.13.

A mixture of 250 mg. of IXb, 80 mg. of 10% palladium–charcoal and 0.1 ml. of concd. sulfuric acid in 20 ml. of ethyl acetate was hydrogenated at room temperature and atmospheric pressure. After hydrogen uptake had ceased the catalyst was filtered, the filtrate extracted with 5% sodium hydroxide solution and the extract acidified and extracted with ether. The ether solution was dried over magnesium sulfate and evaporated. Crystallization of the solid residue from aqueous methanol yielded 230 mg. of crystals, m.p. 146–147°. Recrystallization led to needles of the phenol ester V, m.p., m.m.p. 147.5–148.5°.

5(6)-Dehydro-6-hydroxy-7-ketodehydroabietic Lactone (XIa). (a).—A solution of 0.50 g. of methyl 7-ketodehydroabietate (IXd), 4 ml. of 90% *t*-butyl hydroperoxide and 6 drops of concd. sulfuric acid in 10 ml. of acetic acid was heated at 50–55° for 55 hr. The solution was diluted with water and extracted with ether. The extract was washed with sodium bicarbonate solution and with water, dried over magnesium sulfate and evaporated. The crystalline residue, 0.43 g. (86%), m.p. 186–188°, was crystallized from ethanol yielding colorless needles of the lactone XIa, m.p. 188–189°, $[\alpha]_D$ +4.9° ($CHCl_3$); spectra: ultraviolet (95% ethanol), λ_{max} 262 mμ (log ε 4.09) and 290

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mμ (log ε 4.11); infrared ($CHCl_3$), C=O 5.53(s), 5.95(s), 6.04(s)μ; C=C 6.22(m)μ.

Anal. Calcd. for $C_{20}H_{22}O_3$: C, 77.39; H, 7.14. Found: C, 77.59; H, 7.08.

Oxidations utilizing 97% di-*t*-butyl peroxide or 75% *t*-butyl peracetate (in benzene) as oxidizing agents under identical reaction conditions led to 76 and 50% yields of lactone, respectively.

(b).—A mixture of 250 mg. of methyl 7-ketodehydroabietate (IXd) and 500 mg. of freshly sublimed selenium dioxide in 1 ml. of water and 16 ml. of acetic acid was refluxed for 60 hr. The mixture was filtered and the solvent removed under reduced pressure. Water was added, the mixture extracted with ether and the extract dried over magnesium sulfate and evaporated. Silica chromatography and elution with petroleum ether gave 50 mg. of methyl 5(6)-dehydro-7-ketodehydroabietate (XII) as an oil, $[\alpha]_D$ +42.8° ($CHCl_3$); spectra: ultraviolet (95% ethanol), λ_{max} 255 mμ (log ε 4.06); infrared ($CHCl_3$), C=O 5.82(s), 6.07(s) μ; C=C 6.24(m)μ. Its reddish-orange 2,4-dinitrophenylhydrazone exhibited m.p. 154–155° on crystallization from ethanol.

Anal. Calcd. for $C_{27}H_{30}O_6N_4$: C, 64.02; H, 5.97; N, 11.06. Found: C, 63.86; H, 6.26; N, 11.14.

Elution of the silica chromatogram with 1:1 petroleum ether–benzene yielded 10 mg. of the lactone XIa, m.p. 188–189°, identical in all respects with the lactone above.

(c).—A bromine solution, 0.6 ml. of bromine in 10 ml. of acetic acid, was added with stirring at room temperature to a solution of 1.51 g. of methyl 7-ketodehydroabietate and 1 drop of 15% hydrobromic acid in 5 ml. acetic acid. After 15 min. the solvent was removed under reduced pressure and the residue crystallized from methanol. Three recrystallizations of the product, 1.56 g. (85%), m.p. 151–152°, from methanol gave white needles of methyl 6-bromo-7-ketodehydroabietate, m.p. 153–155°, $[\alpha]_D$ +12.1° ($CHCl_3$); infrared spectrum ($CHCl_3$), C=O 5.82(s), 5.94(s) μ.

Anal. Calcd. for $C_{21}H_{27}O_3Br$: C, 61.92; H, 6.68, Br, 19.62. Found: C, 62.02; H, 6.53; Br, 19.80.

A solution of 160 mg. of the bromoketone in 3 ml. of collidine was refluxed for 18 hr. Water, 7 ml., was added and the mixture extracted with ether. The extract was dried over magnesium sulfate and evaporated. Infrared analysis of the residual oil, 100 mg., revealed the absence of any lactone and the presence of merely crude enone ester XII. Formation of the latter's 2,4-dinitrophenylhydrazone, m.p., m.m.p. 155–156°, confirmed this indication.

A solution of 300 mg. of the bromoketone, 15 ml. of acetonitrile and 15 ml. of dimethyl sulfoxide was refluxed (115°) for 10 days. The solution was poured into water and extracted with ether. The extract was washed with water, dried over magnesium sulfate and evaporated. Three crystallizations of the residual 150 mg. of solid yielded colorless needles of lactone XIa, m.p., m.m.p. 187–188°, spectra identical with those of authentic samples.

Reductions of Lactone XIa. (a) **Hydrogenation.**—A mixture of 105 mg. of lactone XIa, 86 mg. of 10% palladium–charcoal and 0.1 ml. of concd. sulfuric acid in 25 ml. of ethyl acetate was hydrogenated at room temperature and atmospheric pressure. When the reaction ceased after a four-mole uptake of hydrogen, the catalyst was filtered, 5% sodium hydroxide added to the filtrate and the solution extracted with ether. The aqueous solution was acidified and re-extracted with ether. The latter extract was dried over magnesium sulfate and evaporated. Several crystallizations of the residue from methanol gave 95 mg. of dehydroabietic acid, m.p. 165–166° (lit.[20] m.p. 173°), infrared spectrum identical with that of an authentic sample.

(b) **Chemical Reduction.**—A solution of 100 mg. of lactone XIa and 50 mg. of sodium borohydride in 15 ml. of methanol was left standing for 30 min. and then evaporated under reduced pressure. Water was added to the residue and the solution extracted with ether. The extract was dried over magnesium sulfate and evaporated. Three crystallizations of the 80 mg. of residue from ether yielded colorless needles of hydroxylactone XIII, m.p. 232–233°, $[\alpha]_D$ −78.3° ($CHCl_3$); infrared spectrum ($CHCl_3$), OH 2.81(w) μ, C=O 5.66(s) μ, C=C 6.20(s)μ.

Anal. Calcd. for $C_{20}H_{26}O_3$: C, 76.40; H, 8.34. Found: C, 76.51; H, 8.31.

6-Hydroxy-7-ketodehydroabietic Lactone (XIV).—A mixture of 290 mg. of hydroxylactone XIII and 375 mg. of chromic oxide in 3 ml. of water and 15 ml. of acetic acid was allowed to stand at room temperature for 50 min. Saturated brine solution, 50 ml., was added and the mixture extracted with chloroform. The extract was washed with water, dried over magnesium sulfate and evaporated. Chromatography of the crude residue, 220 mg., on 4:1 Bentonite–Celite and elution with 4:1 benzene–carbon tetrachloride gave 160 mg. of a solid, m.p. 215–220°. Four recrystallizations from ethanol yielded colorless needles of ketolactone XIV, m.p. 228–230°, $[\alpha]_D$ +4.0° ($CHCl_3$); spectra: ultraviolet (95% ethanol), λ_{max} 258 mμ (log ε 4.03) and 302 mμ (log ε 3.36); infrared ($CHCl_3$), C=O 5.51(s), 5.90(s) μ; C=C 6.21(w)μ.

Anal. Calcd. for $C_{20}H_{24}O_3$: C, 76.89; H, 7.74. Found: C, 76.83; H, 7.52.

A mixture of 2.2 mg. of lactone XIV 7 mg. of freshly sublimed selenium dioxide in 4 ml. of acetic acid and 3 drops of water was refluxed for 76 hr. The solution was filtered, the solvent removed under reduced pressure and the residue taken up in ether. The organic extract was dried over magnesium sulfate and evaporated. Two crystallizations of the solid residue from ethanol gave 2.1 mg. of lactone XIa, m.p., m.m.p. 187–188°, infrared spectrum identical with that of the lactone product of *t*-butyl hydroperoxide oxidation of methyl 7-ketodehydroabietate (IXd).

(20) L. F. Fieser and W. P. Campbell, *J. Am. Chem. Soc.*, **60**, 2631 (1938).