

Synthesis of Taxodione, Royleanone, Cryptojaponol, and Methyl 11-Hydroxy-12-methoxy-7-oxoabieta-8,11,13-trien-18-oate

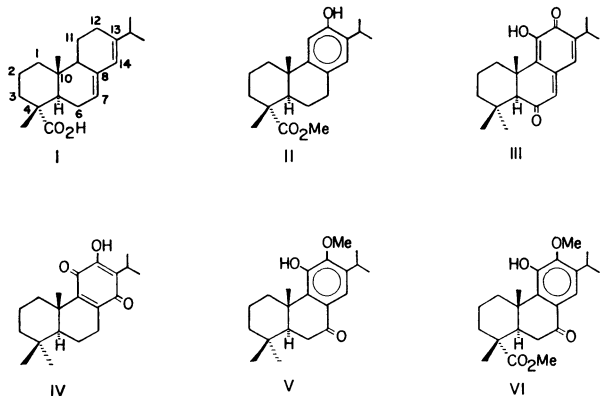
Takashi MATSUMOTO, Yasuo OHSUGA, Shogo HARADA, and Kenji FUKUI

Department of Chemistry, Faculty of Science, Hiroshima University, Higashisenda-machi, Hiroshima 730

(Received August 30, 1976)

Oxidation at the C-11 position of methyl 12-hydroxyabieta-8,11,13-trien-18-oate (II) and ferruginol (XXXII) were successfully carried out using benzoyl peroxide, and the resulting phenols (VII and XXXVII) were further converted into taxodione (III), royleanone (IV), cryptojaponol (V), and methyl 11-hydroxy-12-methoxy-7-oxoabieta-8,11,13-trien-18-oate (VI).

There have been reported the isolation and structural elucidation of many naturally-occurring tricyclic diterpenes possessing an abietane skeleton. As a part of our synthetic studies on natural terpenes, we attempted the conversion of (–)-abietic acid (I) which was easily obtained from pine rosin, into several 11-oxygenated tricyclic diterpenes. This paper¹⁾ describes the conversion of methyl 12-hydroxyabieta-8,11,13-trien-18-oate (II)²⁾ prepared from I into taxodione (III)^{3,4)} which has shown significant tumor-inhibiting activity, royleanone (IV),^{3–7)} cryptojaponol (V),^{4,8,9)} and methyl 11-hydroxy-12-methoxy-7-oxoabieta-8,11,13-trien-18-oate (VI).¹⁰⁾ Since (–)-abietic acid (I) has already been synthesized, the present conversion can be regarded as the total syntheses of these natural compounds (III, IV, V, and VI).

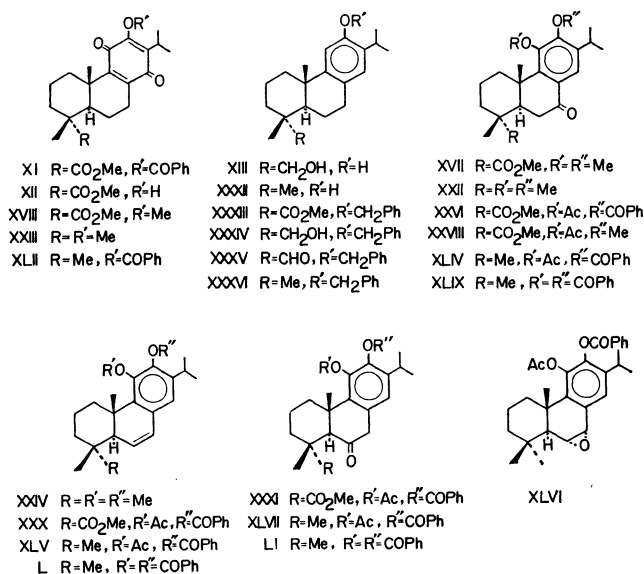


The oxidation of II with benzoyl peroxide in refluxing chloroform afforded a phenol (VII), with three dienones (VIII, IX, and X) as minor products. The structures of these products (VII–X) were assigned on the basis of the following evidence. The phenol (VII) responded positively to the Gibbs test¹⁵⁾ which suggested the presence of an aromatic proton para to a phenolic hydroxyl group. The oxidation of VII with *m*-chloroperbenzoic acid gave a benzoyloxy-*p*-benzoquinone (XI) which was hydrolyzed to give the corresponding hydroxy-*p*-benzoquinone (XII). The NMR spectrum of VII showed a signal at δ 6.57 ppm due to C₁₄-H, while for those of XI and XII no corresponding signal was observed. Thus, the structure of VII was identified to be methyl 12-benzoyloxy-11-hydroxyabieta-8,11,13-trien-18-oate.¹⁶⁾ The treatment of VIII, IX, and X with lithium aluminum hydride in refluxed ether gave the same product, abieta-8,11,13-trien-12,18-diol (XIII).^{17,18)} This suggests that each of these dienones has an oxygen-function at the

C-12 position. From the IR and UV spectra (see Experimental section) of these dienones, it is obvious that IX and X were ortho-substituted dienones,¹⁹⁾ while VIII was a para-substituted dienone.¹⁹⁾ The NMR spectrum of IX was also very similar to that of X, and both IX and X showed two non-equivalent secondary methyl group signals at δ 0.93 and 1.15 ppm and at δ 0.92 and 1.15 ppm, respectively. On the other hand, VIII showed an equivalent signal at δ 1.05 ppm due to the methyls of the isopropyl group. Thus, IX and X should be epimeric isomers with respect to the C-13 position. Hydrolysis of the para-dienone VIII in aqueous methanol with potassium carbonate under reflux gave the corresponding alcohol (XIV). In the NMR spectrum of XIV, the downfield shift of the signal (δ 1.42 ppm) due to the methyl group at the C-10 position relative to the corresponding signal (δ 1.12 ppm) for VIII (or δ 1.17 ppm for II) suggested a 1,3-diaxial-*cis*-relationship between the methyl group and the hydroxyl group at the C-8 position. Thus, the benzoyloxy group in VIII was stereochemically assigned to be the β -configuration. In order to determine the stereochemistry of the benzoyloxy group at the C-13 position in the ortho-dienones IX and X, the following thermal rearrangements were carried out. A solution of X in toluene was refluxed for 2 h to give VII (18%) together with the starting substance (X: 80%). However, a similar treatment of IX gave VII (14%) and VIII (16%) along with IX (67%). From this rearrangement of IX into VIII, the stereochemical structure of the benzoyloxy group in IX was assigned to be the β -configuration, and therefore, that in X to be the α -configuration. The methylation of VII in refluxing methanol with dimethyl sulfate in the presence of aqueous potassium hydroxide gave a monomethyl ether (XV) which responded positively to the Gibbs test. XV was further methylated with dimethyl sulfate and anhydrous potassium carbonate in refluxing methyl ethyl ketones to give methyl 11,12-dimethoxyabieta-8,11,13-trien-18-oate (XVI) which was oxidized with chromium trioxide in acetic acid to afford the corresponding 7-oxo compound (XVII) along with a small amount of methyl 12-methoxy-11,14-dioxoabieta-8,12-dien-18-oate (XVIII). This quinone (XVIII) was also obtained by the oxidation of XV with *m*-chloroperbenzoic acid in a moderate yield. The demethylation of XVIII with hydrochloric acid afforded XII. Subsequently, the conversion of a methoxycarbonyl group at the C-4 position in XVI into a methyl group was carried out in the following manner. The ester XVI was reduced with lithium aluminum hydride to give the

corresponding alcohol (XIX) which by oxidation with a chromium trioxide-pyridine complex gave an aldehyde (XX). Huang-Minlon reduction of XX gave 11,12-dimethoxyabieta-8,11,13-triene (XXI).^{3,11,20} The conversion of XXI into taxodione (III) *via* 11,12-dimethoxyabieta-6,8,11,13-tetraene (XXIV) has been achieved by Mori and Matsui.¹¹ In the present study, XXIV was prepared by an alternate method. The oxidation of XXI with chromium trioxide gave 11,12-dimethoxyabieta-8,11,13-trien-7-one (XXII)^{8,9} together with a small amount of royleanone methyl ether (XXIII)⁵ which was demethylated to give royleanone (IV). The reduction of XXII with lithium aluminum hydride gave the corresponding alcohol which was immediately dehydrated with *p*-toluenesulfonic acid in refluxing toluene to give XXIV.¹¹ The conversion of VII and XV into VI was also carried out as follows. Acetylation of VII with isopropenyl acetate in the presence of *p*-toluenesulfonic acid gave an acetate (XXV),¹⁶ which was then submitted to oxidation with chromium trioxide in acetic acid to give the corresponding 7-oxo derivative (XXVI).¹⁶ Alkaline hydrolysis of XXVI, followed by methylation with diazomethane gave VI. This phenol (VI) was also obtained from XV by a similar treatment *via* an acetate (XXVII) and a ketone (XXVIII). Methyl 11-hydroxy-6,12-dioxoabieta-7,9(11),13-trien-18-oate (XXIX), a taxodione analogue, was also synthesized from XXVI. The reduction of a carbonyl group in XXVI with sodium borohydride and subsequent dehydration of the resulting alcohol gave a tetraene derivative (XXX) which was then oxidized with *m*-chloroperbenzoic acid to give a 6-oxo derivative (XXXI). Alkaline hydrolysis of XXXI followed by oxidation gave XXIX.

Next, the above benzoyl peroxide oxidation was applied to ferruginol (XXXII) which was prepared in the following manner. The treatment of II with benzyl chloride in refluxing *N,N*-dimethylformamide in the presence of anhydrous potassium carbonate gave a benzyl ether (XXXIII), which, on reduction with lithium aluminum hydride followed by oxidation of the resulting alcohol (XXXIV) with a chromium trioxide-pyridine complex, yielded a formyl derivative (XXXV). Huang-Minlon reduction of XXXV gave ferruginol benzyl ether (XXXVI) which was then hydrogenolyzed using Pd-C in acetic acid to give ferruginol (XXXII). The oxidation of XXXII with benzoyl peroxide in chloro-



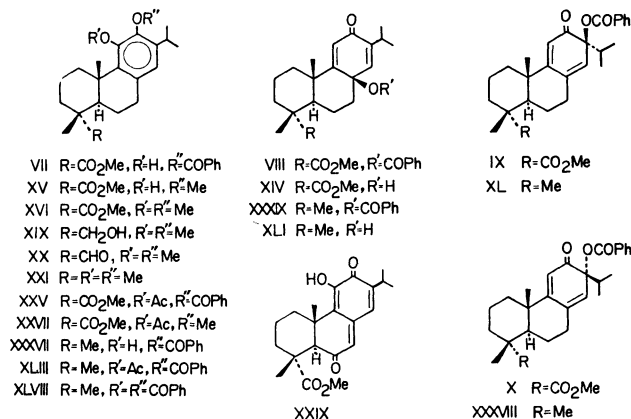
form at room temperature gave a phenol (XXXVII) and three dienones (XXXVIII-XL), whose structures were also assigned on the basis of spectral and chemical studies (see Experimental section), as in the case of VII-X. The phenol XXXVII was easily converted into royleanone (IV) by *m*-chloroperbenzoic acid oxidation and subsequent alkaline hydrolysis *via* royleanone benzoate (XLII). Further, acetylation of XXXVII gave an acetate (XLIII) and this was then oxidized with chromium trioxide in acetic acid to give the corresponding 7-oxo compound (XLIV). The hydrolysis of XLIV followed by methylation with diazomethane gave cryptojaponol (V). Finally, taxodione (III) was also synthesized from the ketone XLIV *via* a tetraene (XLV), an epoxide (XLVI), and a 6-oxo compound (XLVII), and from the phenol XXXVII *via* a dibenzoate (XLVIII),²¹ a 7-oxo compound (XLIX), a tetraene (L), and a 6-oxo compound (LI).

Experimental

All melting points are uncorrected. The IR and UV spectra were taken in chloroform and ethanol, respectively. The NMR spectra were obtained in carbon tetrachloride at 60 MHz with tetramethylsilane as an internal standard, unless otherwise stated. The chemical shifts are presented in the δ values; s: singlet, bs: broad singlet, d: doublet, bd: broad doublet, dd: double doublet, t: triplet, m: multiplet. The optical rotations were measured in chloroform using a Yanaco OR-50D. Column chromatography was performed using Merck silica gel (0.063 mm).

Oxidation of Methyl 12-Hydroxyabieta-8,11,13-trien-18-oate (II) with Benzoyl Peroxide. A solution of the phenol II (5.00 g) and benzoyl peroxide (3.70 g) in chloroform (60 ml) was gently refluxed for 2 h in a stream of nitrogen. The solution was diluted with ether containing a small amount of acetic acid, and washed successively with aqueous potassium iodide, aqueous sodium thiosulfate, aqueous sodium hydrogencarbonate, and water. After drying over sodium sulfate, the solvent was evaporated and the residue was chromatographed on silica gel using benzene and benzene-ether (97:3 and 95:5) as eluents, giving four products (VII-X).

a): Methyl 12-benzoyloxy-11-hydroxyabieta-8,11,13-



trien-18-oate (VII: 61%), which responded positively to the Gibbs test;¹⁵ mp 155–157 °C (from methanol), $[\alpha]_D + 83.1^\circ$, IR: 3575, 3375, 1735, 1718 cm^{-1} , NMR: 1.16 and 1.19 (each d and $J=7$ Hz, $-\text{CH}(\text{CH}_3)_2$), 1.29 (s, C_4-CH_3), 1.38 (s, $\text{C}_{10}-\text{CH}_3$), 3.64 (s, $-\text{CO}_2\text{CH}_3$), 5.26 (s, $-\text{OH}$), 6.57 (s, $\text{C}_{14}-\text{H}$), 7.4–8.2 (m, $-\text{C}_6\text{H}_5$). Found: C, 74.86; H, 7.71%. Calcd for $\text{C}_{28}\text{H}_{34}\text{O}_5$: C, 74.64; H, 7.61%.

b): Methyl 8 β -benzoyloxy-12-oxoabieta-9(11),13-dien-18-oate (VIII: 2%); mp 157–158.5 °C (from methanol), $[\alpha]_D - 81.8^\circ$, IR: 1722, 1668, 1638 cm^{-1} , UV: λ_{max} 236 nm (ϵ 18600), NMR: 1.05 (d, $J=7$ Hz, $-\text{CH}(\text{CH}_3)_2$), 1.12 (s, $\text{C}_{10}-\text{CH}_3$), 1.22 (s, C_4-CH_3), 3.65 (s, $-\text{CO}_2\text{CH}_3$), 6.11 and 6.25 (each s, $\text{C}_{11}-\text{H}$ and $\text{C}_{14}-\text{H}$), 7.2–8.1 (m, $-\text{C}_6\text{H}_5$). Found: C, 74.46; H, 7.67%. Calcd for $\text{C}_{28}\text{H}_{34}\text{O}_5$: C, 74.64; H, 7.61%.

c): Methyl 13 β -benzoyloxy-12-oxoabieta-8(14),9(11)-dien-18-oate (IX: 6%); mp 140–141 °C (from methanol), $[\alpha]_D - 196^\circ$, IR: 1715, 1663 cm^{-1} , UV: λ_{max} nm (ϵ) 232 (19800), 321 (2280), NMR (CDCl_3): 0.93 and 1.15 (each d and $J=7$ Hz, $-\text{CH}(\text{CH}_3)_2$), 1.28 (s, C_4-CH_3 and $\text{C}_{10}-\text{CH}_3$), 3.68 (s, $-\text{CO}_2\text{CH}_3$), 5.92 (bs, $\text{C}_{14}-\text{H}$), 6.07 (s, $\text{C}_{11}-\text{H}$), 7.2–8.2 (m, $-\text{C}_6\text{H}_5$). Found: C, 74.37; H, 7.65%. Calcd for $\text{C}_{28}\text{H}_{34}\text{O}_5$: C, 74.64; H, 7.61%.

d): Methyl 13 α -benzoyloxy-12-oxoabieta-8(14),9(11)-dien-18-oate (X: 11%); mp 167–168 °C (from methanol), $[\alpha]_D + 280^\circ$, IR: 1715, 1663 cm^{-1} , UV: λ_{max} nm (ϵ) 232 (19700), 321 (2740), NMR (CDCl_3): 0.92 and 1.15 (each d and $J=7$ Hz, $-\text{CH}(\text{CH}_3)_2$), 1.23 and 1.29 (each s, C_4-CH_3 and $\text{C}_{10}-\text{CH}_3$), 3.67 (s, $-\text{CO}_2\text{CH}_3$), 5.90 (bs, $\text{C}_{14}-\text{H}$), 6.07 (s, $\text{C}_{11}-\text{H}$), 7.2–8.2 (m, $-\text{C}_6\text{H}_5$). Found: C, 74.34; H, 7.75%. Calcd for $\text{C}_{28}\text{H}_{34}\text{O}_5$: C, 74.64; H, 7.61%.

Methyl 12-Benzoyloxy-11,14-dioxoabieta-8,12-dien-18-oate (XI). A solution of VII (360 mg) and *m*-chloroperbenzoic acid (290 mg) in dichloromethane (15 ml) was allowed to stand at room temperature for 22 h and then diluted with ether. The solution was washed successively with aqueous potassium iodide, aqueous sodium thiosulfate, aqueous sodium hydrogencarbonate, and water. After drying over sodium sulfate, the solvent was evaporated and the crude product was purified by column chromatography on silica gel using benzene as the eluent producing the recovered VII (104 mg: 29%) and a quinone (XI) (166 mg: 45%), which was recrystallized from ethanol; mp 121–123 °C, $[\alpha]_D + 32.4^\circ$, IR: 1740, 1720, 1658, 1646 sh, 1602 cm^{-1} , UV: λ_{max} nm (ϵ) 235.5 (17300), 264.5 (17700), NMR: 1.22 (s, C_4-CH_3), 1.22 and 1.25 (each d and $J=7$ Hz, $-\text{CH}(\text{CH}_3)_2$), 1.30 (s, $\text{C}_{10}-\text{CH}_3$), 3.64 (s, $-\text{CO}_2\text{CH}_3$), 7.4–8.3 (m, $-\text{C}_6\text{H}_5$). Found: C, 72.39; H, 7.02%. Calcd for $\text{C}_{28}\text{H}_{32}\text{O}_6$: C, 72.39; H, 6.94%.

Methyl 12-Hydroxy-11,14-dioxoabieta-8,12-dien-18-oate (XII). a): A mixture of XI (110 mg), sodium hydrogencarbonate (500 mg), water (4 ml), and methanol (20 ml) was refluxed for 1 h. After removal of the solvent, the residue was extracted with ether, washed with water, and then dried over sodium sulfate. The crude product was chromatographed on silica gel (20 g) using benzene–ether (99:1) as the eluent to give XII (53 mg; 62%), which was recrystallized from petroleum ether; mp 149–150 °C, $[\alpha]_D + 93.1^\circ$, IR: 3375, 1720, 1640, 1633, 1603 cm^{-1} , NMR: 1.20 (d, $J=7$ Hz, $-\text{CH}(\text{CH}_3)_2$), 1.22 (s, C_4-CH_3), 1.28 (s, $\text{C}_{10}-\text{CH}_3$), 3.66 (s, $-\text{CO}_2\text{CH}_3$), 7.15 (s, $-\text{OH}$). Found: C, 69.95; H, 7.77%. Calcd for $\text{C}_{21}\text{H}_{28}\text{O}_5$: C, 69.97; H, 7.83%.

b): A mixture of methyl 12-methoxy-11,14-dioxoabieta-8,12-dien-18-oate (XVIII: 113 mg) and concentrated hydrochloric acid (5 ml) in methanol (15 ml) was refluxed for 15 h. After the usual work-up, the product was purified using column chromatography and subsequent crystallization to give XII (mp 149–150 °C) which was shown to be identical to a sample of a) from a comparison of the IR and NMR spectra.

Reductions of Dienones (VIII, IX, and X) with Lithium Aluminum Hydride.

a): A mixture of VIII (100 mg) and lithium aluminum hydride (100 mg) in dry ether (15 ml) was refluxed for 1.5 h. After the usual work-up, the product was recrystallized from a mixture of acetone and petroleum ether to give abieta-8,11,13-trien-12,18-diol (XIII: 60 mg),^{17,18} mp 180–181 °C, $[\alpha]_D + 72.1^\circ$ (ethanol), which was identical to an authentic sample prepared from II by lithium aluminum hydride reduction. Found: C, 79.71; H, 10.05%. Calcd for $\text{C}_{20}\text{H}_{30}\text{O}_2$: C, 79.42; H, 10.00%.

b): Each of the benzoates (IX and X) was also reduced with lithium aluminum hydride as described in a) above producing XIII.

Methyl 8 β -Hydroxy-12-oxoabieta-9(11),13-dien-18-oate (XIV).

A mixture of VIII (65 mg), potassium carbonate (200 mg), water (2 ml), and methanol (8 ml) was refluxed for 2 h. After the usual work-up, the crude product was chromatographed on silica gel (20 g) using benzene–ether (9:1) as the eluent to give XIV (46 mg: 92%) which was recrystallized from a mixture of ether and petroleum ether; mp 74–77 °C, $[\alpha]_D - 60.0^\circ$, IR: 3588, 3413, 1720, 1665, 1635 cm^{-1} , UV: λ_{max} 241 nm (ϵ 12900), NMR: 1.00 and 1.04 (each d and $J=7$ Hz, $-\text{CH}(\text{CH}_3)_2$), 1.27 (s, C_4-CH_3), 1.42 (s, $\text{C}_{10}-\text{CH}_3$), 3.64 (s, $-\text{CO}_2\text{CH}_3$), 5.81 and 6.28 (each s, $\text{C}_{11}-\text{H}$ and $\text{C}_{14}-\text{H}$).

Thermal Rearrangement of Dienones (IX and X). a): A solution of IX (100 mg) in toluene (3 ml) was refluxed for 2 h and the crude product, after evaporation of the solvent, was purified by column chromatography on silica gel (20 g) using benzene–ether (99:1) as the eluent giving VII (14 mg: 14%), VIII (16 mg: 16%), and the recovered IX (67 mg: 67%).

b): A solution of X (130 mg) in toluene (3 ml) was refluxed for 2 h. Chromatographic purification gave VII (23 mg: 18%) and the recovered X (103 mg: 80%).

Methyl 11-Hydroxy-12-methoxyabieta-8,11,13-trien-18-oate (XV). A mixture of VII (2.5 g), 30% aqueous potassium hydroxide (4.5 ml), and methanol (50 ml) was refluxed for 10 min in a stream of nitrogen. To the cold solution, dimethyl sulfate (4.5 ml) was added and the mixture was refluxed for 4.5 h. The reaction mixture was further treated with 30% aqueous potassium hydroxide under reflux for 20 min, cooled, acidified with dilute hydrochloric acid, and then extracted with ether. After the usual work-up, the product was chromatographed on silica gel (300 g) using benzene as the eluent and recrystallized from methanol giving XV (1.6 g: 80%), mp 146–147 °C, $[\alpha]_D + 68.8^\circ$, IR: 3500, 1720 cm^{-1} , NMR: 1.20 (d, $J=7$ Hz, $-\text{CH}(\text{CH}_3)_2$), 1.24 (s, C_4-CH_3), 1.32 (s, $\text{C}_{10}-\text{CH}_3$), 3.61 (s, $-\text{CO}_2\text{CH}_3$), 3.69 (s, $-\text{OCH}_3$), 5.85 (s, $-\text{OH}$), 6.30 (s, $\text{C}_{14}-\text{H}$). Found: C, 73.07; H, 8.96%. Calcd for $\text{C}_{22}\text{H}_{32}\text{O}_4$: C, 73.30; H, 8.95%. The phenol XV responded positively to the Gibbs test.¹⁵

Methyl 11,12-Dimethoxyabieta-8,11,13-trien-18-oate (XVI).

A mixture of XV (136 mg), anhydrous potassium carbonate (5 g), dimethyl sulfate (0.6 ml), and methyl ethyl ketone (20 ml) was refluxed for 24 h. After the usual work-up, the product was chromatographed on silica gel (30 g) using benzene as the eluent and recrystallized from methanol giving XVI (134 mg: 95%), mp 92–92.5 °C, $[\alpha]_D + 82.8^\circ$, NMR: 1.16 and 1.18 (each d and $J=7$ Hz, $-\text{CH}(\text{CH}_3)_2$), 1.24 (s, C_4-CH_3), 1.30 (s, $\text{C}_{10}-\text{CH}_3$), 3.60 (s, $-\text{CO}_2\text{CH}_3$), 3.68 and 3.79 (each s, 2- OCH_3), 6.46 (s, $\text{C}_{14}-\text{H}$). Found: C, 73.80; H, 9.14%. Calcd for $\text{C}_{23}\text{H}_{34}\text{O}_4$: C, 73.76; H, 9.15%.

Methyl 12-Methoxy-11,14-dioxoabieta-8,12-dien-18-oate (XVIII).

A solution of XV (210 mg) and *m*-chloroperbenzoic acid (220 mg) in dichloromethane (10 ml) was treated as described above for XI. The crude product was purified by column chromatography on silica gel (20 g) with benzene giving XVIII (128 mg: 59%) which was recrystallized from

petroleum ether; mp 139–140 °C, $[\alpha]_D -70.7^\circ$, IR: 1718, 1653, 1638, 1600 cm^{-1} , NMR: 1.16 (bd, $J=7$ Hz, $-\text{CH}(\text{CH}_3)_2$), 1.20 (s, C_4-CH_3), 1.30 (s, $\text{C}_{10}-\text{CH}_3$), 3.58 (s, $-\text{CO}_2-\text{CH}_3$), 3.82 (s, $-\text{OCH}_3$). Found: C, 70.85; H, 8.16%. Calcd for $\text{C}_{22}\text{H}_{30}\text{O}_5$: C, 70.56; H, 8.08%.

Oxidation of XVI with Chromium Trioxide. A mixture of XVI (183 mg) and chromium trioxide (90 mg) in acetic acid (4 ml) was allowed to stand at room temperature for 18 h and then diluted with ether. The mixture was washed successively with water, aqueous sodium hydrogencarbonate, and water. After removal of the solvent, the residue was chromatographed on silica gel (20 g) using benzene–ether (97:3) as the eluent to give a quinone (29 mg; 16%) which was shown to be identical to XVIII from IR and NMR spectral comparisons. Further elution gave a ketone (XVII) (147 mg; 77%) which was recrystallized from petroleum ether; mp 101.5–102 °C, $[\alpha]_D +48.1^\circ$, IR: 1720, 1675 cm^{-1} , NMR: 1.22 and 1.26 (each d and $J=7$ Hz, $-\text{CH}(\text{CH}_3)_2$), 1.30 (s, C_4-CH_3), 1.39 (s, $\text{C}_{10}-\text{CH}_3$), 3.62 (s, $-\text{CO}_2-\text{CH}_3$), 3.77 and 3.78 (each s, 2- OCH_3), 7.60 (s, $\text{C}_{14}-\text{H}$). Found: C, 70.84; H, 8.53%. Calcd for $\text{C}_{22}\text{H}_{30}\text{O}_5$: C, 71.10; H, 8.30%.

11,12-Dimethoxyabieta-8,11,13-trien-18-ol (XIX). A mixture of XVI (393 mg) in dry ether (10 ml) and lithium aluminum hydride (80 mg) was refluxed for 2 h. After the usual work-up, the product was chromatographed on silica gel (40 g) using benzene–ether (99:1) as the eluent to give an alcohol (XIX: 380 mg), $[\alpha]_D +79.7^\circ$, IR: 3620, 3450 cm^{-1} , NMR: 0.81 (s, C_4-CH_3), 1.13 and 1.18 (each d and $J=6.5$ Hz, $-\text{CH}(\text{CH}_3)_2$), 1.28 (s, $\text{C}_{10}-\text{CH}_3$), 3.65 and 3.75 (each s, 2- OCH_3), 6.42 (s, $\text{C}_{14}-\text{H}$).

11,12-Dimethoxyabieta-8,11,13-triene (XXI). a): A solution of XIX (380 mg) in pyridine (6 ml) was added to the Sarett reagent prepared from chromium trioxide (450 mg) and pyridine (6 ml). The mixture was stirred at room temperature for 50 min and then filtered. The filtrate was acidified with dilute hydrochloric acid, extracted with ether, and the extract was washed with brine. The crude product was purified by column chromatography on silica gel (40 g) using hexane–benzene (1:9) as the eluent to give an aldehyde (XX) (234 mg; 62%), $[\alpha]_D +73.5^\circ$, IR: 1718 cm^{-1} , NMR: 1.13 (s, C_4-CH_3), 1.16 and 1.18 (each d and $J=7$ Hz, $-\text{CH}(\text{CH}_3)_2$), 1.32 (s, $\text{C}_{10}-\text{CH}_3$), 3.68 and 3.78 (each s, 2- OCH_3), 6.47 (s, $\text{C}_{14}-\text{H}$), 9.17 (s, $-\text{CHO}$).

b): A mixture of XX (234 mg) in diethylene glycol (6 ml) and 80% hydrazine hydrate (0.6 ml) was refluxed for 2 h and powdered sodium hydroxide (0.6 g) was then added. The mixture was heated at 200 °C for 3 h, cooled, extracted with ether, and the extract was washed with brine. Removal of the solvent and subsequent chromatography on silica gel (20 g) using hexane–benzene (1:9) as the eluent gave XXI (179 mg; 80%); mp 89.5–90.5 °C, $[\alpha]_D +92.0^\circ$ (EtOH), NMR (CDCl_3): 0.93 (s, $-\text{C}(\text{CH}_3)_2$), 1.18 and 1.21 (each d and $J=7$ Hz, $-\text{CH}(\text{CH}_3)_2$), 1.30 (s, $\text{C}_{10}-\text{CH}_3$), 3.70 and 3.78 (each s, 2- OCH_3), 6.55 (s, $\text{C}_{14}-\text{H}$). Found: C, 79.74; H, 10.25%. Calcd for $\text{C}_{22}\text{H}_{34}\text{O}_2$: C, 79.95; H, 10.37%.

Oxidation of XXI with Chromium Trioxide. A solution of XXI (570 mg) and chromium trioxide (300 mg) in acetic acid (20 ml) was allowed to stand at room temperature for 48 h. After the mixture had been treated as described above, the product was chromatographed on silica gel (150 g) and eluted with benzene to give a small amount of royleanone methyl ether (XXIII)⁹ (19 mg; 3%) which was recrystallized from methanol; mp 117.5–118.5 °C, $[\alpha]_D -113^\circ$, IR: 1654, 1643, 1602 cm^{-1} , NMR: 0.92 (s, $-\text{C}(\text{CH}_3)_2$), 1.17 and 1.19 (each d and $J=7$ Hz, $-\text{CH}(\text{CH}_3)_2$), 1.30 (s, $\text{C}_{10}-\text{CH}_3$), 3.86 (s, $-\text{OCH}_3$).

Further elution with benzene–ether (98:2) gave 11,12-di-

methoxyabieta-8,11,13-trien-7-one (XXII)^{8,9} (406 mg; 64%); $[\alpha]_D +35.5^\circ$, IR: 1672 cm^{-1} , NMR: 1.00 (s, $-\text{C}(\text{CH}_3)_2$), 1.21 and 1.27 (each d and $J=7$ Hz, $-\text{CH}(\text{CH}_3)_2$), 1.38 (s, $\text{C}_{10}-\text{CH}_3$), 3.80 (s, 2- OCH_3), 7.60 (s, $\text{C}_{14}-\text{H}$).

11,12-Dimethoxyabieta-6,8,11,13-tetraene (XXIV). A mixture of XXII (203 mg) in dry ether (10 ml) and lithium aluminum hydride (40 mg) was refluxed for 2 h. After the usual work-up, the crude alcohol was further treated under reflux with *p*-toluenesulfonic acid (20 mg) in toluene (20 ml) for 3 h, and then cooled. After the addition of sodium hydrogencarbonate, the mixture was stirred for 30 min, filtered, and the filtrate was evaporated. The crude product was chromatographed on silica gel (50 g) using hexane–benzene (1:1) as the eluent producing XXIV¹¹ (165 mg; 85%), $[\alpha]_D -99.6^\circ$, NMR (CDCl_3): 0.96 and 1.03 (each s, $-\text{C}(\text{CH}_3)_2$), 1.13 (s, $\text{C}_{10}-\text{CH}_3$), 1.18 and 1.22 (each d and $J=7$ Hz, $-\text{CH}(\text{CH}_3)_2$), 2.19 (t, $J=3$ Hz, C_5-H), 3.77 (s, 2- OCH_3), 5.86 (dd, $J=3$ and 9 Hz, C_6-H), 6.41 (dd, $J=3$ and 9 Hz, C_7-H), 6.63 (s, $\text{C}_{14}-\text{H}$). Found: C, 80.18; H, 9.88%. Calcd for $\text{C}_{22}\text{H}_{32}\text{O}_2$: C, 80.44; H, 9.83%.

Methyl 11-Acetoxy-12-benzoyloxyabieta-8,11,13-trien-18-oate (XXV). A mixture of VII (300 mg) in toluene (4 ml), *p*-toluenesulfonic acid (30 mg), and isopropenyl acetate (0.6 ml) was refluxed for 5 h. After the usual work-up, the product was recrystallized from methanol containing a small amount of acetone producing XXV (300 mg; 92%), mp 191–192 °C, $[\alpha]_D +88.7^\circ$, IR: 1763, 1740, 1720 cm^{-1} , NMR: 1.78 (s, $-\text{OCOCH}_3$). Found: C, 72.92; H, 7.36%. Calcd for $\text{C}_{30}\text{H}_{36}\text{O}_6$: C, 73.14; H, 7.37%.

Methyl 11-Acetoxy-12-benzoyloxy-7-oxoabieta-8,11,13-trien-18-oate (XXVI). A mixture of XXV (700 mg) and chromium trioxide (350 mg) in acetic acid was allowed to stand at room temperature for 26 h. The crude product was chromatographed on silica gel (70 g) and eluted with benzene–ether (95:5) giving XXVI (586 mg; 82%), mp 178–180 °C (from methanol), $[\alpha]_D +72.0^\circ$, IR: 1765, 1738, 1720, 1682 cm^{-1} , NMR: 7.95 (s, $\text{C}_{14}-\text{H}$). Found: C, 70.85; H, 6.71%. Calcd for $\text{C}_{30}\text{H}_{34}\text{O}_7$: C, 71.13; H, 6.77%.

Methyl 11-Hydroxy-12-methoxy-7-oxoabieta-8,11,13-trien-18-oate (VI). a): A mixture of XXVI (135 mg) in methanol (7 ml) and 30% aqueous potassium hydroxide (0.6 ml) was refluxed for 2 h in a stream of nitrogen. After removal of the solvent, the residue was acidified, extracted with ether, and the extract was washed with water. The crude product was methylated with diazomethane and then chromatographed on silica gel (20 g) using benzene–ether (99:1) as the eluent giving VI¹⁰ (68 mg; 68%), which was recrystallized from petroleum ether containing a small amount of acetone; mp 202.5–203.5 °C, $[\alpha]_D +33.8^\circ$, IR (CCl_4): 3500, 1730, 1685, 1607 cm^{-1} , NMR (CDCl_3): 1.25 (d, $J=7$ Hz, $-\text{CH}(\text{CH}_3)_2$), 1.32 (s, C_4-CH_3), 1.41 (s, $\text{C}_{10}-\text{CH}_3$), 3.62 (s, $-\text{CO}_2\text{CH}_3$), 3.78 (s, $-\text{OCH}_3$), 6.13 (s, $-\text{OH}$), 7.59 (s, $\text{C}_{14}-\text{H}$). Found: C, 70.51; H, 8.12%. Calcd for $\text{C}_{22}\text{H}_{30}\text{O}_5$: C, 70.56; H, 8.08%.

b): Similarly, XV (109 mg) was acetylated with isopropenyl acetate (0.1 ml) and *p*-toluenesulfonic acid (10 mg) in toluene (5 ml) giving the corresponding acetate (XXVII) (94 mg; 77%), IR: 1760, 1720 cm^{-1} .

Oxidation of XXVII (94 mg) with chromium trioxide (50 mg) in acetic acid (3 ml) gave methyl 11-acetoxy-12-methoxy-7-oxoabieta-8,11,13-trien-18-oate (XXVIII) (71 mg; 73%), IR: 1760, 1720, 1680 cm^{-1} , which was then hydrolyzed under reflux for 2 h with 30% aqueous potassium hydroxide (0.3 ml) in methanol (7 ml) yielding VI (44 mg; 69%). IR and NMR spectra of the synthetic VI were identical with those of a natural sample.

Methyl 11-Acetoxy-12-benzoyloxyabieta-6,8,11,13-tetraen-18-oate (XXX). A mixture of XXVI (1.26 g) in methanol

(20 ml) and sodium borohydride (190 mg) was allowed to stand at 0 °C for 3.5 h. After the usual work-up, the crude alcohol (1.26 g) was refluxed with *p*-toluenesulfonic acid (130 mg) in toluene (40 ml) for 1.5 h. The product was chromatographed on silica gel (120 g) using benzene-ether (99:1) as the eluent giving XXX (1.11 g: 91%), which was recrystallized from ethanol; mp 128–129 °C, $[\alpha]_D +29.3^\circ$, IR: 1758, 1735, 1720 cm^{-1} , NMR: 3.03 (t, $J=2.5$ Hz, $\text{C}_5\text{-H}$), 5.59 (dd, $J=2.5$ and 9.5 Hz, $\text{C}_6\text{-H}$), 6.42 (dd, $J=2.5$ and 9.5 Hz, $\text{C}_7\text{-H}$). Found: C, 73.36; H, 6.99%. Calcd for $\text{C}_{30}\text{H}_{34}\text{O}_6$: C, 73.45; H, 6.99%.

Methyl 11-Acetoxy-12-benzoyloxy-6-oxoabieta-8,11,13-trien-18-oate (XXXI). A mixture of XXX (210 mg) in dichloromethane (20 ml) and *m*-chloroperbenzoic acid (88 mg) was allowed to stand at 0 °C for 4 h, and then extracted with ether. The ether extract was washed with aqueous sodium hydrogen carbonate and water. Evaporation of the solvent and subsequent chromatography on silica gel (20 g) using benzene-ether (98:2) as the eluent gave XXXI (46 mg: 22%), which was recrystallized from a mixture of acetone and methanol; mp 253–255 °C, $[\alpha]_D +164^\circ$, IR: 1760, 1732, 1725, 1710 cm^{-1} , NMR (CDCl_3): 1.23 and 1.25 (each d and $J=7$ Hz, $-\text{CH}(\text{CH}_3)_2$), 1.28 and 1.47 (each s, $\text{C}_4\text{-CH}_3$ and $\text{C}_{10}\text{-CH}_3$), 1.96 (s, $-\text{OCOCH}_3$), 3.48 (s, $\text{C}_5\text{-H}$), 3.65 (s, $-\text{CO}_2\text{CH}_3$), 3.71 (s, $-\text{COCH}_2-$), 7.00 (s, $\text{C}_{14}\text{-H}$), 7.3–8.4 (m, $-\text{C}_6\text{H}_5$). Found: C, 70.85; H, 6.81%. Calcd for $\text{C}_{30}\text{H}_{34}\text{O}_7$: C, 71.13; H, 6.77%.

Methyl 11-Hydroxy-6,12-dioxoabieta-7,9(11),13-trien-18-oate (XXIX). A mixture of XXXI (298 mg) in methanol (54 ml), sodium hydrogencarbonate (200 mg), and water (6 ml) was refluxed for 40 min, and then extracted with ether. The extract was washed with water, dried over sodium sulfate, and evaporated. The crude product was chromatographed on silica gel (20 g) using benzene-ether (99:1) as the eluent giving XXIX (127 mg: 61%), which was recrystallized from methanol; mp 57.5–59 °C, $[\alpha]_D -80.3^\circ$, IR: 3345, 1723, 1667, 1642, 1627, 1617, 1600 cm^{-1} , UV: λ_{max} nm (ϵ) 325 (20000), 335 (21400), 405 (3020), NMR: 1.22 (d, $J=7$ Hz, $-\text{CH}(\text{CH}_3)_2$), 1.32 (s, $\text{C}_4\text{-CH}_3$), 1.46 (s, $\text{C}_{10}\text{-CH}_3$), 3.49 (s, $\text{C}_5\text{-H}$), 3.66 (s, $-\text{CO}_2\text{CH}_3$), 6.21 (s, $\text{C}_7\text{-H}$), 6.92 (s, $\text{C}_{14}\text{-H}$), 7.62 (s, $-\text{OH}$).

Methyl 12-Benzoyloxyabieta-8,11,13-trien-18-oate (XXXIII). A mixture of II (500 mg) in *N,N*-dimethylformamide (2 ml), benzyl chloride (250 mg), and anhydrous potassium carbonate (2 g) was refluxed with stirring for 1 h, cooled, diluted with ether, and then acidified with dilute hydrochloric acid. The ether solution was washed with brine, dried over sodium sulfate, and evaporated. The residue was chromatographed on silica gel using benzene as the eluent giving XXXIII (617 mg: 97%), which was recrystallized from ethanol, mp 76.5–77 °C, $[\alpha]_D +70.4^\circ$. Found: C, 80.13; H, 8.57%. Calcd for $\text{C}_{28}\text{H}_{36}\text{O}_3$: C, 79.96; H, 8.63%.

12-Benzoyloxyabieta-8,11,13-trien-18-one (XXXV). A mixture of XXXIII (4.60 g) in dry ether (50 ml) and lithium aluminum hydride (1.0 g) was refluxed for 4 h. After the usual work-up, the crude alcohol XXXIV (4.05 g) in pyridine (40 ml) was oxidized at room temperature for 1.5 h with Sarett reagent prepared from chromium trioxide (3.09 g) and pyridine (30 ml). The product was recrystallized from ethanol giving XXXV (2.13 g: 69%), mp 135–136.5 °C, $[\alpha]_D +73.9^\circ$, IR: 1720 cm^{-1} , NMR: 9.15 (s, $-\text{CHO}$). Found: C, 82.83; H, 8.64%. Calcd for $\text{C}_{27}\text{H}_{34}\text{O}_2$: C, 83.03; H, 8.78%.

12-Benzoyloxyabieta-8,11,13-triene (Ferruginol Benzyl Ether) (XXXVI). A mixture of XXXV (2.06 g) in diethylene glycol (62 ml) and 80% hydrazine hydrate (8.2 ml) was refluxed for 2 h. After the addition of powdered sodium hydroxide (8.2 g), the mixture was further heated at 195–200 °C for 3 h. After the usual work-up, the product was purified by

column chromatography on silica gel (200 g) using hexane-benzene (1:3) as the eluent giving XXXVI (1.82 g: 92%), which was recrystallized from ethanol, mp 63–64 °C, $[\alpha]_D +68.2^\circ$. Found: C, 86.37; H, 9.80%. Calcd for $\text{C}_{27}\text{H}_{36}\text{O}$: C, 86.11; H, 9.64%.

Ferruginol (XXXII). A mixture of XXXVI (2.26 g) in acetic acid (150 ml), 5% Pd-C (750 mg), and concentrated hydrochloric acid (1.0 ml) was stirred at room temperature for ca. 3 h in an atmosphere of hydrogen. After the usual work-up, the product was chromatographed on silica gel (150 g) using hexane-benzene (2:3) as the eluent giving XXXII (1.69 g: 98%), $[\alpha]_D +57.5^\circ$, IR: 3605, 3350 cm^{-1} , NMR: 0.90 and 0.92 (each s, $-\text{C}(\text{CH}_3)_2$), 1.08 (s, $\text{C}_{10}\text{-CH}_3$), 1.17 (d, $J=7$ Hz, $-\text{CH}(\text{CH}_3)_2$), 5.18 (s, $-\text{OH}$), 6.37 and 6.65 (each s, $\text{C}_{11}\text{-H}$ and $\text{C}_{14}\text{-H}$).

Oxidation of Ferruginol (XXXII) with Benzoyl Peroxide. A solution of XXXII (5.73 g) and benzoyl peroxide (5.60 g) in chloroform (30 ml) was allowed to stand at room temperature for 4 h. The crude product was purified by column chromatography on silica gel giving four products (XXXVII–XL).

a): 12-Benzoyloxyabieta-8,11,13-trien-11-ol (XXXVII: 44%), which responded positively to Gibbs test;¹⁵⁾ mp 132.5–133 °C (from petroleum ether), $[\alpha]_D +81.2^\circ$, IR: 3575, 3350, 1740 cm^{-1} , NMR: 0.97 (s, $-\text{C}(\text{CH}_3)_2$), 1.17 and 1.19 (each d and $J=7$ Hz, $-\text{CH}(\text{CH}_3)_2$), 1.33 (s, $\text{C}_{10}\text{-CH}_3$), 5.17 (s, $-\text{OH}$), 6.50 (s, $\text{C}_{14}\text{-H}$), 7.4–8.3 (m, $-\text{C}_6\text{H}_5$). Found: C, 80.02; H, 8.56%. Calcd for $\text{C}_{27}\text{H}_{34}\text{O}_3$: C, 79.76; H, 8.43%.

b): 12-Oxoabieta-8(14),9(11)-dien-13 α -yl benzoate (XXXVIII: 6%); mp 134.5–135.5 °C (from methanol), $[\alpha]_D +270^\circ$, IR: 1714, 1664 cm^{-1} , UV: λ_{max} nm (ϵ) 233 (15400), 321 (2230), NMR: 0.90 and 1.11 (each d and $J=7$ Hz, $-\text{CH}(\text{CH}_3)_2$), 0.96 (s, $-\text{C}(\text{CH}_3)_2$), 1.19 (s, $\text{C}_{10}\text{-CH}_3$), 5.81 and 5.89 (each s, $\text{C}_{11}\text{-H}$ and $\text{C}_{14}\text{-H}$), 7.2–8.1 (m, $-\text{C}_6\text{H}_5$). Found: C, 79.56; H, 8.55%. Calcd for $\text{C}_{27}\text{H}_{34}\text{O}_3$: C, 79.76; H, 8.43%.

c): 12-Oxoabieta-9(11),13-dien-8 β -yl benzoate (XXXIX: 2%); mp 139–140 °C (from methanol), $[\alpha]_D -119^\circ$, IR: 1721, 1665, 1630 cm^{-1} , UV: λ_{max} 235 nm (ϵ 20900), NMR: 0.92 (s, $-\text{C}(\text{CH}_3)_2$), 1.05 (d, $J=7$ Hz, $-\text{CH}(\text{CH}_3)_2$), 1.11 (s, $\text{C}_{10}\text{-CH}_3$), 6.09 and 6.26 (each s, $\text{C}_{11}\text{-H}$ and $\text{C}_{14}\text{-H}$). Found: C, 79.60; H, 8.51%. Calcd for $\text{C}_{27}\text{H}_{34}\text{O}_3$: C, 79.76; H, 8.43%.

d): 12-Oxoabieta-8(14),9(11)-dien-13 β -yl benzoate (XL: 3%); mp 135–136 °C (from methanol), $[\alpha]_D -214^\circ$, IR: 1715, 1663 cm^{-1} , UV: λ_{max} nm (ϵ) 233 (17000), 321 (2350), NMR: 0.88 and 1.11 (each d and $J=7$ Hz, $-\text{CH}(\text{CH}_3)_2$), 0.94 and 0.97 (each s, $-\text{C}(\text{CH}_3)_2$), 1.27 (s, $\text{C}_{10}\text{-CH}_3$), 5.80 and 5.88 (each s, $\text{C}_{11}\text{-H}$ and $\text{C}_{14}\text{-H}$), 7.2–8.1 (m, $-\text{C}_6\text{H}_5$). Found: C, 80.03; H, 8.63%. Calcd for $\text{C}_{27}\text{H}_{34}\text{O}_3$: C, 79.76; H, 8.43%.

Reduction of XXXVIII, XXXIX, and XL with Lithium Aluminum Hydride. A mixture of XXXVIII (83 mg) in dry ether (5 ml) and lithium aluminum hydride (100 mg) was refluxed for 1.5 h. After the usual work-up, the product was purified by column chromatography to give ferruginol (XXXII) (53 mg: 91%).

By similar treatments, XXXIX and XL were also converted to XXXII.

Thermal Rearrangement of Dienones (XXXVIII and XL).

a): A solution of XXXVIII (119 mg) in toluene (5 ml) was refluxed for 2 h, and then evaporated. The residue was chromatographed on silica gel to give XXXVII (8 mg: 7%) and the recovered XXXVIII (106 mg: 89%).

b): A similar treatment of XL (129 mg) in refluxing toluene (5 ml) for 2 h gave XXXVII (22 mg: 17%), XXXIX (15 mg: 12%), and the recovered XL (86 mg: 67%).

8 β -Hydroxyabieta-9(11),13-dien-12-one (XLI). A mixture of XXXIX (90 mg) in methanol (16 ml), anhydrous potassium carbonate (200 mg), and water (2 ml) was refluxed

for 2 h and the solvent was removed in a vacuum. After the residue had been extracted with ether, the extract was washed with water, dried, and then evaporated. The crude product was chromatographed on silica gel (20 g) using benzene-ether (95:5) as the eluent to give the recovered XXXIX (14 mg: 16%) and an alcohol (XLI) (56 mg: 83%), which was recrystallized from methanol, mp 181–182.5 °C, $[\alpha]_D -142^\circ$, IR: 3580, 3400, 1662, 1630 cm^{-1} , UV: λ_{max} 242 nm (ϵ 12700), NMR (CDCl_3): 0.90 and 0.95 (each s, $-\text{C}(\text{CH}_3)_2$), 1.05 (d, $J=7$ Hz, $-\text{CH}(\text{CH}_3)_2$), 1.38 (s, $\text{C}_{10}-\text{CH}_3$), 1.86 (s, $-\text{OH}$), 5.98 and 6.38 (each s, $\text{C}_{11}-\text{H}$ and $\text{C}_{14}-\text{H}$). Found: C, 79.40; H, 10.12%. Calcd for $\text{C}_{20}\text{H}_{30}\text{O}_2$: C, 79.42; H, 10.00%.

12-Benzoyloxyabieta-8,12-dien-11,14-dione (Royleanone Benzoate) (XLII).

A solution of XXXVII (205 mg) and *m*-chloroperbenzoic acid (155 mg) in dichloromethane (7 ml) was allowed to stand at room temperature for 25 h. After the usual work-up, the crude product was chromatographed on silica gel (30 g) using hexane-benzene (1:1) as the eluent to give the recovered XXXVII (78 mg: 38%) and XLII (100 mg: 45%), which was recrystallized from ethanol; mp 196–197 °C, $[\alpha]_D +52.3^\circ$, IR: 1740, 1659 cm^{-1} , UV: λ_{max} nm (ϵ) 235 (15900), 265 (16400), NMR: 0.93 (s, $-\text{C}(\text{CH}_3)_2$), 1.24 (d, $J=7$ Hz, $-\text{CH}(\text{CH}_3)_2$), 1.28 (s, $\text{C}_{10}-\text{CH}_3$), 7.4–8.2 (m, $-\text{C}_6\text{H}_5$). Found: C, 76.88; H, 7.66%. Calcd for $\text{C}_{27}\text{H}_{32}\text{O}_4$: C, 77.11; H, 7.67%.

Royleanone (IV). a): A mixture of the benzoate XLII (96 mg) in methanol (40 ml), sodium hydrogencarbonate (300 mg), and water (7 ml) was refluxed for 1 h. After removal of the solvent under vacuum, the residue was extracted with ether and the extract was washed with water, dried, and then evaporated. The crude product was chromatographed on silica gel using benzene as the eluent to give royleanone (IV)⁵ (62 mg: 84%), which was recrystallized from hexane; mp 181.5–183 °C, $[\alpha]_D +137^\circ$, IR: 3375, 1674, 1636, 1602 cm^{-1} , UV: λ_{max} nm (ϵ) 277 (14100), 403 (440), NMR: 0.95 (s, $-\text{C}(\text{CH}_3)_2$), 1.20 (d, $J=7$ Hz, $-\text{CH}(\text{CH}_3)_2$), 1.26 (s, $\text{C}_{10}-\text{CH}_3$), 7.16 (s, $-\text{OH}$). Found: C, 76.21; H, 9.04%. Calcd for $\text{C}_{20}\text{H}_{28}\text{O}_3$: C, 75.91; H, 8.92%.

b): A solution of the methyl ether XXIII (31.8 mg) in methanol (5 ml) and 10% hydrochloric acid (1.0 ml) was refluxed for 16 h. After the usual work-up, the product was purified by column chromatography to give royleanone (IV) (11.7 mg: 38%), mp 180.5–182 °C. The IR and NMR spectra of the synthetic royleanone were identical to those of a natural sample.

11-Acetoxy-12-benzoyloxyabieta-8,11,13-triene (XLIII). A solution of XXXVII (710 mg) in dry toluene (10 ml), *p*-toluenesulfonic acid (40 mg), and isopropenyl acetate (2 ml) was refluxed for 5 h. After the usual work-up, the crude product was chromatographed on silica gel (70 g) using benzene as the eluent to give XLIII (730 mg: 93%), which was recrystallized from methanol; mp 179–179.5 °C, $[\alpha]_D +80.0^\circ$, IR: 1760, 1738 cm^{-1} , NMR: 0.91 and 0.96 (each s $-\text{C}(\text{CH}_3)_2$), 1.18 and 1.20 (each d and $J=7$ Hz, $-\text{CH}(\text{CH}_3)_2$), 1.26 (s, $\text{C}_{10}-\text{CH}_3$), 1.81 (s, $-\text{OCOCH}_3$), 6.82 (s, $\text{C}_{14}-\text{H}$), 7.2–8.3 (m, $-\text{C}_6\text{H}_5$). Found: C, 77.36; H, 8.01%. Calcd for $\text{C}_{29}\text{H}_{36}\text{O}_4$: C, 77.64; H, 8.09%.

11-Acetoxy-12-benzoyloxyabieta-8,11,13-trien-7-one (XLIV). A solution of XLIII (985 mg) in acetic acid (20 ml) was oxidized with chromium trioxide (450 mg) at room temperature for 22 h. The product was purified by column chromatography on silica gel (100 g) using benzene-ether (99:1) as the eluent to give XLIV (833 mg: 82%), which was recrystallized from ethanol; mp 160–162 °C, $[\alpha]_D +56.9^\circ$, IR: 1768, 1740, 1680 cm^{-1} , NMR: 0.98 (s, $-\text{C}(\text{CH}_3)_2$), 1.25 and 1.29 (each d and $J=7$ Hz, $-\text{CH}(\text{CH}_3)_2$), 1.34 (s, $\text{C}_{10}-\text{CH}_3$), 1.87 (s, $-\text{OCOCH}_3$), 7.5–8.3 (m, $-\text{C}_6\text{H}_5$), 7.98 (s, $\text{C}_{14}-\text{H}$). Found:

C, 75.54; H, 7.44%. Calcd for $\text{C}_{29}\text{H}_{34}\text{O}_5$: C, 75.30; H, 7.41%.

Cryptojaponol (V). A mixture of XLIV (250 mg) in methanol (18 ml), sodium hydrogencarbonate (600 mg), and water (2 ml) was refluxed for 1 h. After the usual work-up, the crude product was methylated with diazomethane and then purified by column chromatography on silica gel (20 g) using benzene-ether (99:1) as the eluent to give cryptojaponol (V)^{8,9} (145 mg: 81%), which was recrystallized from methanol; mp 205–206.6 °C, $[\alpha]_D +20.0^\circ$, IR: 3505, 1670, 1605 cm^{-1} , NMR: 0.98 (s, $-\text{C}(\text{CH}_3)_2$), 1.26 (d, $J=7$ Hz, $-\text{CH}(\text{CH}_3)_2$), 1.39 (s, $\text{C}_{10}-\text{CH}_3$), 3.77 (s, $-\text{OCH}_3$), 6.02 (s, $-\text{OH}$), 7.48 (s, $\text{C}_{14}-\text{H}$). Found: C, 76.09; H, 9.13%. Calcd for $\text{C}_{21}\text{H}_{30}\text{O}_3$: C, 76.32; H, 9.15%.

11-Acetoxy-12-benzoyloxyabieta-6,8,11,13-tetraene (XLV). A solution of XLIV (263 mg) and sodium borohydride (120 mg) in methanol (7 ml) was allowed to stand at 0 °C for 4 h. After the usual work-up, the product (251 mg) was dehydrated with *p*-toluenesulfonic acid (90 mg) in dry toluene (15 ml) under reflux for 3.5 h to afford a tetraene derivative along with the corresponding 11-hydroxy-12-benzoyloxy derivative. The above mixture was then acetylated with isopropenyl acetate (1 ml) in the presence of *p*-toluenesulfonic acid (20 mg) in refluxing toluene (10 ml) and chromatographed on silica gel to give XLV (148 mg: 56%), which was recrystallized from methanol; mp 157–158 °C, $[\alpha]_D -80.8^\circ$, IR: 1758, 1737 cm^{-1} , NMR: 0.98 and 1.02 (each s, $-\text{C}(\text{CH}_3)_2$), 1.15 (s, $\text{C}_{10}-\text{CH}_3$), 1.20 and 1.24 (each d and $J=7$ Hz, $-\text{CH}(\text{CH}_3)_2$), 1.84 (s, $-\text{OCOCH}_3$), 2.32 (t, $J=2.5$ Hz, C_5-H), 5.92 (dd, $J=2.5$ and 9.5 Hz, C_6-H), 6.48 (dd, $J=2.5$ and 9.5 Hz, C_7-H), 6.84 (s, $\text{C}_{14}-\text{H}$), 7.4–8.3 (m, $-\text{C}_6\text{H}_5$). Found: C, 78.15; H, 7.59%. Calcd for $\text{C}_{29}\text{H}_{34}\text{O}_4$: C, 77.99; H, 7.67%.

11-Acetoxy-12-benzoyloxyabieta-8,11,13-trien-6-one (XLVII). A solution of XLV (589 mg) and *m*-chloroperbenzoic acid (320 mg) in dichloromethane (10 ml) was allowed to stand at room temperature for 24 h. After the usual work-up, the crude epoxide was chromatographed on silica gel (60 g) using benzene-ether (99:1) as the eluent to give XLVII (475 mg: 78%), which was recrystallized from methanol; 222–224 °C, $[\alpha]_D +111^\circ$, IR: 1762, 1740, 1717 cm^{-1} , NMR: 1.05 and 1.30 (each s, $-\text{C}(\text{CH}_3)_2$), 1.19 and 1.23 (each d and $J=7$ Hz, $-\text{CH}(\text{CH}_3)_2$), 1.30 (s, $\text{C}_{10}-\text{CH}_3$), 1.87 (s, $-\text{OCOCH}_3$), 2.64 (s, C_5-H), 3.60 (bs, $-\text{COCH}_2-$), 6.90 (s, $\text{C}_{14}-\text{H}$), 7.5–8.3 (m, $-\text{C}_6\text{H}_5$). Found: C, 75.06; H, 7.54%. Calcd for $\text{C}_{29}\text{H}_{34}\text{O}_5$: C, 75.30; H, 7.41%.

The above crude epoxide was recrystallized from a mixture of acetone and petroleum ether giving pure epoxide (XLVI), mp 199–201 °C, $[\alpha]_D +6.5^\circ$, IR: 1765, 1740 cm^{-1} , NMR (CDCl_3): 1.13 (s, $-\text{C}(\text{CH}_3)_2$), 1.21 and 1.26 (each d and $J=7$ Hz, $-\text{CH}(\text{CH}_3)_2$), 1.33 (s, $\text{C}_{10}-\text{CH}_3$), 1.93 (s, $-\text{OCOCH}_3$), 3.54 (t, $J=4.5$ Hz, C_6-H), 3.92 (d, $J=4.5$ Hz, C_7-H), 7.38 (s, $\text{C}_{14}-\text{H}$), 7.4–8.3 (m, $-\text{C}_6\text{H}_5$). Found: C, 75.45; H, 7.49%. Calcd for $\text{C}_{29}\text{H}_{34}\text{O}_5$: C, 75.30; H, 7.41%.

11,12-Bis(benzoyloxy)abieta-8,11,13-triene (XLVIII). A solution of XXXVII (244 mg), benzoyl chloride (0.2 ml), and pyridine (4 ml) was heated at 80–100 °C for 2 h. The product was purified by column chromatography on silica gel using benzene as the eluent to give XLVIII²¹ (279 mg: 91%), which was recrystallized from a mixture of acetone and petroleum ether; mp 207–208 °C, $[\alpha]_D +76.2^\circ$, IR: 1735 cm^{-1} , NMR: 0.92 and 0.97 (each s, $-\text{C}(\text{CH}_3)_2$), 1.22 (d, $J=7$ Hz, $-\text{CH}(\text{CH}_3)_2$), 1.28 (s, $\text{C}_{10}-\text{CH}_3$), 6.90 (s, $\text{C}_{14}-\text{H}$), 7.0–8.1 (m, $2-\text{C}_6\text{H}_5$). Found: C, 79.82; H, 7.53%. Calcd for $\text{C}_{34}\text{H}_{38}\text{O}_4$: C, 79.97; H, 7.50%.

11,12-Bis(benzoyloxy)abieta-8,11,13-trien-7-one (XLIX). A solution of XLVIII (8.40 g) in acetic acid (300 ml) was oxidized at room temperature for 24 h with chromium trioxide

(7.0 g). The crude product was purified by chromatography on silica gel (300 g) using benzene as the eluent to give XLIX (6.15 g; 69%), which was recrystallized from methanol; mp 150–151 °C, $[\alpha]_D +23^\circ$, IR: 1742, 1682 cm^{-1} , NMR: 8.03 (s, $\text{C}_{14}\text{-H}$). Found: C, 77.56; H, 6.94%. Calcd for $\text{C}_{34}\text{H}_{36}\text{O}_5$: C, 77.83; H, 6.92%.

11,12-Bis(benzoyloxy)abieta-6,8,11,13-tetraene (L). A solution of XLIX (5.55 g) in methanol (120 ml) was reduced at 0 °C for 4 h with sodium borohydride (1.2 g). The crude alcohol was then dehydrated for 2 h with *p*-toluenesulfonic acid (1.8 g) in refluxing toluene (100 ml). The product was purified by chromatography on silica gel (300 g) using hexane–benzene (1:9) as the eluent to give L (4.40 g; 76%), which was recrystallized from a mixture of acetone and methanol; mp 182.5–183 °C, $[\alpha]_D -308^\circ$, IR: 1740 cm^{-1} , NMR: 2.33 (t, $J=3$ Hz, $\text{C}_5\text{-H}$), 5.96 (dd, $J=3$ and 9.5 Hz, $\text{C}_6\text{-H}$), 6.52 (dd, $J=3$ and 9.5 Hz, $\text{C}_7\text{-H}$). Found: C, 80.55; H, 7.24%. Calcd for $\text{C}_{34}\text{H}_{36}\text{O}_4$: C, 80.28; H, 7.13%.

11,12-Bis(benzoyloxy)abieta-8,11,13-trien-6-one (LI). A solution of L (501 mg) in chloroform (5 ml) was treated at room temperature for 3 h with *m*-chloroperbenzoic acid (207 mg). The epoxide was chromatographed on silica gel (50 g) using benzene–ether (98:2) as the eluent to give LI (340 mg; 66%), which was recrystallized from a mixture of acetone and methanol; mp 207–208 °C, $[\alpha]_D +58.3^\circ$, IR: 1740, 1718 cm^{-1} , NMR: 1.04 and 1.30 (each s, $-\dot{\text{C}}(\text{CH}_3)_2$), 1.25 (d, $J=7$ Hz, $-\text{CH}(\text{CH}_3)_2$), 1.30 (s, $\text{C}_{10}\text{-CH}_3$), 2.65 (s, $\text{C}_5\text{-H}$), 3.64 (bs, $-\text{COCH}_2-$), 6.93 (s, $\text{C}_{14}\text{-H}$), 7.0–8.1 (m, 2- C_6H_5). Found: C, 78.12; H, 7.03%. Calcd for $\text{C}_{34}\text{H}_{36}\text{O}_5$: C, 77.83; H, 6.92%.

Taxodione (III). a): A mixture of XLVII (150 mg) in methanol (10 ml), sodium hydrogencarbonate (450 mg), and water (1 ml) was refluxed for 1 h. The crude phenol was chromatographed on silica gel (20 g) using benzene as the eluent to give taxodione (III) (62 mg; 60%), which was recrystallized from petroleum ether; mp 97.5–98 °C, $[\alpha]_D +40^\circ$, IR: 3345, 1671, 1642, 1626, 1614, 1598 cm^{-1} , UV: λ_{max} nm (ϵ) 323 (23400), 335 (24500), 405 (3240), Mass: m/e 314 (M^+), NMR (CDCl_3): 1.12 and 1.27 (each s, $-\dot{\text{C}}(\text{CH}_3)_2$), 1.18 (d, $J=7$ Hz, $-\text{CH}(\text{CH}_3)_2$), 1.27 (s, $\text{C}_{10}\text{-CH}_3$), 2.61 (s, $\text{C}_5\text{-H}$), 2.96 (m, $-\text{CH}(\text{CH}_3)_2$), 6.20 (s, $\text{C}_7\text{-H}$), 6.87 (s, $\text{C}_{14}\text{-H}$), 7.57 (s, $-\text{OH}$). Found: C, 76.23; H, 8.39%. Calcd for $\text{C}_{20}\text{H}_{26}\text{O}_3$: C, 76.40; H, 8.34%.

b): A mixture of LI (340 mg) in methanol (25 ml), sodium hydrogencarbonate (1.0 g), and water (7 ml) was treated as described under a) above to give taxodione (III) (120 mg; 59%). The IR and NMR spectra of the synthetic taxodione were identical with those of a natural sample.

The authors are grateful to Arakawa Rinsan Kogyo Co., Ltd. for a generous gift of rosin. Thanks are also due to Professor S. Morris Kupchan, University of

Virginia, to Professor O. E. Edwards, National Research Council, Ottawa, and to Professor J. F. Biellmann, Institute of Louis Pasteur, for kindly supplying the natural samples and their spectra.

References

- 1) A part of this work has been reported in preliminary form: T. Matsumoto, Y. Ohsuga, and K. Fukui, *Chem. Lett.*, **1974**, 297.
- 2) R. C. Cambie and R. A. Franich, *Aust. J. Chem.*, **24**, 117 (1971).
- 3) S. M. Kupchan, A. Karim, and C. Marcks, *J. Am. Chem. Soc.*, **90**, 5923 (1968); *J. Org. Chem.*, **34**, 3912 (1969).
- 4) Taxodione,^{11,12} royleanone,^{5,13,14} and cryptojaponol⁹ have previously been synthesized by different methods as optically-active or racemic forms.
- 5) O. E. Edwards, G. Feniak, and M. Los, *Can. J. Chem.*, **40**, 1540 (1962).
- 6) J. H. Gough and M. D. Sutherland, *Aust. J. Chem.*, **19**, 329 (1966).
- 7) C. H. Eugster, *Palette*, **1968**, 25; *Chem. Abstr.*, **69**, 54262e (1968).
- 8) T. Kondo, M. Suda, and M. Teshima, *Yakugaku Zasshi*, **82**, 1252 (1962).
- 9) E. Wenkert, J. D. McChesney, and D. J. Watts, *J. Org. Chem.*, **35**, 2422 (1970).
- 10) J. F. Biellmann, G. Branlant, M. Gero-Robert, and M. Poiret, *Tetrahedron*, **29**, 1237 (1973).
- 11) K. Mori and M. Matsui, *Tetrahedron*, **26**, 3467 (1970).
- 12) T. Matsumoto, Y. Tachibana, J. Uchida, and K. Fukui, *Bull. Chem. Soc. Jpn.*, **44**, 2766 (1971).
- 13) a) T. Matsumoto, Y. Tachibana, and K. Fukui, *Chem. Lett.*, **1972**, 321; b) Y. Tachibana, *Bull. Chem. Soc. Jpn.*, **48**, 298 (1975).
- 14) T. Matsui, *J. Sci. Hiroshima Univ. Ser. A*, **40**, 129 (1976).
- 15) F. E. King, T. J. King, and L. C. Manning, *J. Chem. Soc.*, **1957**, 563.
- 16) In a previous communication,¹ these substances were formulated as 11-benzoyloxy derivatives. This should now be revised to 12-benzoyloxy compounds.
- 17) I. Fukushima, Y. Sayama, K. Kyogoku, and H. Murayama, *Agric. Biol. Chem.*, **32**, 1103 (1968).
- 18) L. F. Fieser and W. P. Campbell, *J. Am. Chem. Soc.*, **61**, 2528 (1939).
- 19) D. H. R. Barton, P. D. Magnus, and M. J. Pearson, *J. Chem. Soc., C*, **1971**, 2231.
- 20) C. H. Brieskorn, A. Fuchs, J. B. Bredenberg, J. D. McChesney, and E. Wenkert, *J. Org. Chem.*, **29**, 2293 (1964).
- 21) C. P. Falshaw, A. W. Johnson, and T. J. King, *J. Chem. Soc.*, **1963**, 2422.