The Total Synthesis of (+)-Taxoquinone, (−)-7α-Acetoxyroyleanone, (−)-Dehydroroyleanone, (−)-Horminone, (−)-7-Oxoroyleanone, and (+)-Inuroyleanol

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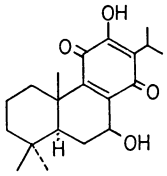
Methylation of 12-benzoyloxyabieta-8,11,13-trien-11-ol with methyl iodide afforded 11-benzoyloxy-12-methoxyabieta- and 12-benzoyloxy-11-methoxyabieta-8,11,13-triene (**9**). Oxidation of the latter product with chromium trioxide, followed by sodium borohydride reduction and acetylation, gave 7β-acetoxy-12-benzoyloxy-11-methoxyabieta-8,11,13-triene (**17**) and its 7α-acetoxy isomer (**18**) in a ratio of *ca.* 5 : 1. On the other hand, treatment of **9** with lead tetraacetate produced **17** and **18** in a ratio of *ca.* 1 : 2. The 7β-acetate (**17**) was then oxidized with chromium trioxide and the resulting *p*-quinone derivative was hydrolyzed with aqueous sodium hydroxide to give taxoquinone (**1**), which on dehydration gave dehydroroyleanone. Similarly, the 7α-acetate (**18**) was converted into horminone (**4**) *via* the *p*-quinone derivative, which was treated with aqueous sodium hydrogencarbonate to give 7α-acetoxyroyleanone. Oxidation of **4** with manganese dioxide afforded 7-oxoroyleanone. Methylation of **1** with diazomethane, followed by oxidation with a chromium trioxide–pyridine complex, afforded 12-methoxyabieta-8,12-diene-7,11,14-trione, which on reduction with sodium dithionite gave inuroyleanol.

There have been reports on the isolation and structural elucidation of many naturally-occurring highly-oxygenated tricyclic diterpenes possessing an oxygen function at the C-11 position. In previous papers,[1,2] we reported the successful oxidation of the C-11 position in the tricyclic C ring-aromatized diterpenes with benzoyl peroxide. As an extension of that work, our efforts were further directed toward the syntheses of highly-oxygenated tricyclic diterpenes possessing an abietane skeleton. This paper[3] describes the syntheses of (+)-taxoquinone (**1**),[4,5] (−)-7α-acetoxyroyleanone (**2**),[6,7] (−)-dehydroroyleanone (**3**),[5,6,8,9] (−)-horminone (**4**),[5,10] (−)-7-oxoroyleanone (**5**),[5,7] and (+)-inuroyleanol (**6**),[7] all starting from (+)-ferruginol (**7**). Since the total synthesis of optically active ferruginol[11] has recently been accomplished in our laboratory, the present work constitutes the total syntheses of all the above natural diterpenes (**1**—**6**).

The oxidation of ferruginol (**7**) with benzoyl peroxide in chloroform afforded 12-benzoyloxyabieta-8,11,13-trien-11-ol (**8**)[2] which was methylated with methyl iodide and anhydrous potassium carbonate in refluxing ethyl methyl ketone to give the two monomethyl ethers, **9** and **10**, in a ratio of *ca.* 3 : 2. In order to elucidate the structures of these two products, the minor product (**10**) was reduced with lithium aluminium hydride in ether to yield a phenol (**11**) which responded positively to the Gibbs test,[12] suggesting the presence of an aromatic proton para to a phenolic hydroxyl group. Therefore, the structure of **10** was determined as 11-benzoyloxy-12-methoxyabieta-8,11,13-triene.[13] This structure was further confirmed by the following conversion. The oxidation of **10** with chromium trioxide in acetic acid produced the corresponding 7-oxo compound (**12**), which on alkaline hydrolysis gave cryptojaponol (**13**).[2,14] The major product (**9**) was then hydrolyzed with aqueous sodium hydroxide in refluxing methanol to give another phenol (**14**) which, in contrast with **11**, showed a negative Gibbs test,[12] suggesting the presence of a substituent para to a phenolic hydroxyl group. Therefore, the structure of **9** was assigned as 12-benzoyloxy-11-methoxyabieta-8,11,13-triene. The compound **9** was also oxidized with chromium trioxide in acetic acid to give the corresponding 7-oxo compound (**15**) together with the *p*-benzoquinone derivative, which was identical with 12-benzoyloxyabieta-8,12-diene-11,14-dione (**16**)[2] prepared from **8** by oxidation with *m*-chloroperbenzoic acid. The reduction of **15** with sodium borohydride in methanol at 0 °C followed by acetylation of the resulting mixture of epimeric alcohols with acetic anhydride in pyridine at room temperature produced a mixture of 7β-acetoxy-12-benzoyloxy-11-methoxyabieta-8,11,13-triene (**17**) and its 7α-acetoxy isomer (**18**) in a ratio of *ca.* 5 : 1. The stereochemistry of the acetoxyl group was established on the basis of the C-7 proton signals with half-height width of 15 Hz at δ 5.93 ppm in **17** and 5 Hz at δ 5.86 ppm in **18** in their NMR spectra. This reaction procedure leading to the 7-acetoxy compounds (**17** and **18**) is



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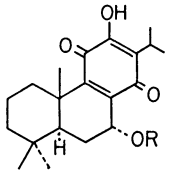
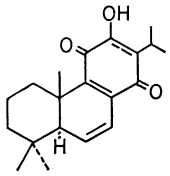


2 R=Ac
4 R=H



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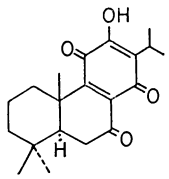

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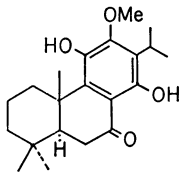

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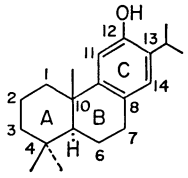

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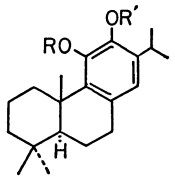
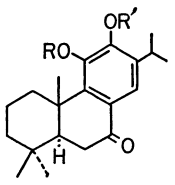
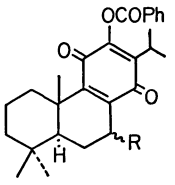
suitable for the synthesis of taxoquinone (**1**) possessing a 7β-hydroxyl group. However, for the syntheses of 7α-acetoxyroyleanone (**2**) and horminone (**4**) it is necessary to prepare **18** predominantly. For this purpose, the direct acetoxylation on the C-7 position in **9** was carried out with lead tetraacetate in refluxing acetic acid in a stream of nitrogen. The chromatographic purification of the crude porduct on silica gel afforded a mixture of **17** and **18** in a ratio of *ca.* 1 : 2. The 7β-acetate (**17**) was then oxidized with chromium trioxide in acetic acid at room temperature to yield 7β-acetoxy-12-benzoyloxyabieta-8,12-diene-11,14-dione (**19**) along with the 7-oxo compound (**15**). The hydrolysis of **19** with aqueous sodium hydroxide in refluxing methanol, followed by treatment with dilute hydrochloric acid, afforded taxoquinone (**1**). This was dehydrated[5] with *p*-toluenesulfonic acid in refluxing benzene to give dehydroroyleanone (**3**) and also methylated[5] with diazomethane to give 7β-hydroxy-12-methoxyabieta-8,12-diene-11,14-dione (**20**). Similarly, the 7α-acetate (**18**) was oxidized with chromium trioxide in acetic acid to give 7α-acetoxy-12-benzoyloxyabieta-8,12-diene-11,14-dione (**21**) along with the 7-oxo compound (**15**). The treatment of **21** first with aqueous sodium hydroxide in refluxing methanol, followed with dilute hydrochloric acid, produced horminone (**4**) which on oxidation[5] with manganese dioxide in dioxane afforded 7-oxoroyleanone (**5**). On the other hand, when **21** was hydrolyzed with aqueous sodium hydrogencarbonate in refluxing methanol, 7α-acetoxyroyleanone (**2**) was obtained. The hydroxyquinone (**20**) was then oxidized with a chromium trioxide–pyridine complex to give 12-methoxyabieta-8,12-diene-7,11,14-trione (**22**), which was reduced at 95 °C with sodium dithionite in acetic acid to afford inuroyleanol (**6**).



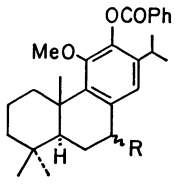
8 R=H, R'=COPh
9 R=Me, R'=COPh
10 R=COPh, R'=Me
11 R=H, R'=Me
14 R=Me, R'=H



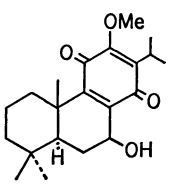
12 R=COPh, R'=Me
13 R=H, R'=Me
15 R=Me, R'=COPh



16 R=H
19 R=β-OAc
21 R=α-OAc



17 R=β-OAc
18 R=α-OAc



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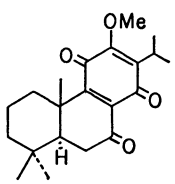

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Experimental

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 terms of δ values; s: 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).

Methylation of 12-Benzoyloxyabieta-8,11,13-trien-11-ol (8). A mixture of **8**[2] (10.00 g), methyl iodide (16.0 ml), and anhydrous potassium carbonate (40.0 g) in ethyl methyl ketone (50 ml) was refluxed for 8 h. The mixture was cooled to room temperature, poured into water, and extracted with ether. The ether extract was washed with brine, dried over sodium sulfate, and then evaporated *in vacuo*. The residue was chromatographed on silica gel (300 g) using benzene as the eluent to give 12-benzoyloxy-11-methoxyabieta-8,11,13-triene (**9**) (6.25 g: 60%) which was recrystallized from ether–methanol: mp 125—126 °C; $[\alpha]_D$+76.4°; IR: 1735 cm^{-1}; NMR: 0.95 (6H, s, $-\overset{|}{C}(CH_3)_2$), 1.15 and 1.17 (each 3H, d, and J=7 Hz, $-CH(C\underline{H}_3)_2$), 1.30 (3H, s, C_{10}–CH_3), 3.68 (3H, s, $-OCH_3$), 6.67 (1H, s, C_{14}–H), 7.3—8.3 (5H, m, aromatic protons). Found: C, 80.03; H, 8.45%. Calcd for $C_{28}H_{36}O_3$: C, 79.96; H, 8.63%.

Further elution gave 11-benzoyloxy-12-methoxyabieta-8,11,13-triene (**10**) (3.95 g: 38%) which was recrystallized from chloroform–acetone: mp 183.5—184.5 °C; $[\alpha]_D$+76.5°; IR: 1735 cm^{-1}; NMR: 0.91 and 0.96 (each 3H and s, $-\overset{|}{C}-(CH_3)_2$), 1.22 (6H, d, J=7 Hz, $-CH(C\underline{H}_3)_2$), 1.39 (3H, s, C_{10}–CH_3), 3.52 and 3.57 (each *ca.* 1.5 H and s, $-OCH_3$),[15] 6.74 (1H, s, C_{14}–H), 7.3—8.4 (5H, m, aromatic protons). Found: C, 80.24; H, 8.55%. Calcd for $C_{28}H_{36}O_3$: C, 79.96; H, 8.63%.

12-Methoxyabieta-8,11,13-trien-11-ol (11). A mixture of **10** (208 mg) and lithium aluminium hydride (300 mg) in dry ether (15 ml) was refluxed for 2 h. The mixture was poured into ice–dilute hydrochloric acid and extracted with ether. The ether extract was washed with water, dried over sodium sulfate, and then evaporated *in vacuo*. The residue was chromatographed on silica gel (15 g) using benzene as the eluent to give **11** (126 mg: 80%) which responded positively to the Gibbs test.[12] Mp 94—94.5 °C (from methanol); $[\alpha]_D$+67.2°; IR: 3510 cm^{-1}; NMR : 0.94(6H, s, $-\overset{|}{C}(CH_3)_2$), 1.18 (6H, d, J=7 Hz, $-CH(C\underline{H}_3)_2$), 1.28 (3H, s, C_{10}–CH_3), 3.70 (3H, s, $-OCH_3$), 5.79 (1H, s, C_{11}–OH), 6.25 (1H, s, C_{14}–H). Found: C, 79.92; H, 10.21%. Calcd for $C_{21}H_{32}O_2$: C, 79.70; H, 10.19%.

11-Benzoyloxy-12-methoxyabieta-8,11,13-trien-7-one (12). A mixture of **10** (2.00 g) and chromium trioxide (2.00 g) in acetic acid (60 ml) was allowed to stand at room temperature for 24 h. The mixture was poured into ether–aqueous sodium hydrogencarbonate and extracted with ether. The ether extract was washed with brine, dried over sodium sulfate, and then evaporated *in vacuo*. The crude product was chromatographed on silica gel (200 g) using ether–benzene (5 : 95) as the eluent to give **12**[14] (1.24 g: 60%) which was recrystallized from chlroroform–ether : mp 197—198 °C; $[\alpha]_D$+68.9°; IR: 1739, 1676 cm^{-1}; NMR: 0.97 (6H, s, $-\overset{|}{C}(CH_3)_2$), 1.25(3H, s, C_{10}–CH_3), 1.26 and 1.39 (each 3H, d, and J=7 Hz, $-CH(C\underline{H}_3)_2$), 2.56 (2H, bd, J=7 Hz, $-CH_2CO-$), 3.61 and 3.65 (each *ca.* 1.5 H and s, $-OCH_3$),[14] 7.85 (1H, s, C_{14}–H), 7.3—8.3 (5H, m, aromatic protons). Found: C, 77.10; H, 7.85%. Calcd for $C_{28}H_{34}O_4$: C, 77.39; H, 7.89%.

Cryptojaponol (13). A mixture of **12** (600 mg) and 10% aqueous sodium hydroxide (5.0 ml) in methanol (35 ml)

was refluxed for 1 h and then evaporated *in vacuo*. The residue was acidified with dilute hydrochloric acid and extracted with ether. The ether extract was washed successively with water, aqueous sodium hydrogencarbonate, and brine. The dried solution was then evaporated *in vacuo* to afford a solid which was recrystallized from methanol, giving **13** (180 mg), mp 205—207 °C. Found: C, 76.21; H, 9.08%. Calcd for $C_{21}H_{30}O_3$: C, 76.32; H, 9.15%. The mother liquor of crystallization was evaporated *in vacuo* and the residue was chromatographed on silica gel (20 g) using ether–benzene (1 : 99) as the eluent to give an additional **13** (106 mg). The IR and NMR spectra of **13** were identical with those of authentic cryptojaponol.[2]

11-Methoxyabieta-8,11,13-trien-12-ol (14). A mixture of **9** (171 mg) and 10% aqueous sodium hydroxide (1.5 ml) in methanol (10 ml) was refluxed for 1 h. After the same work-up as described for the preparation of **13**, the crude product was chromatographed on silica gel (15 g) using benzene as the eluent to give **14** (124 mg: 80%) which responded negatively to the Gibbs test.[12] Mp 114.5—115 °C (from methanol); $[\alpha]_D$+67.5°; IR: 3545, 3340 cm^{-1}; NMR: 0.95 (6H, s, $-\dot{C}(CH_3)_2$), 1.20 (6H, d, J=7 Hz, $-CH(C\underline{H}_3)_2$), 1.28 (3H, s, $C_{10}-CH_3$), 3.74 (3H, s, $-OCH_3$), 5.18 (1H, s, $C_{12}-OH$), 6.48 (1H, s, $C_{14}-H$). Found: C, 79.98; H, 10.21%. Calcd for $C_{21}H_{32}O_2$: C, 79.70; H, 10.19%.

Oxidation of 9 with Chromium Trioxide. Chromium trioxide (6.0 g) was added to a stirred solution of **9** (5.959 g) in acetic acid (80 ml) over a 1 h period. The mixture was further stirred at room temperature for 5 h and then allowed to stand for 18 h. The mixture was poured into water and extracted with ether. The ether extract was washed successively with water, aqueous sodium hydrogencarbonate, and brine. After drying over sodium sulfate, the solvent was evaporated *in vacuo* and the residue was chromatographed on silica gel (300 g) using benzene as the eluent to give 12-benzoyloxyabieta-8,12-diene-11,14-dione (**16**) (1.630 g: 27%) which was recrystallized from ethanol: mp 196—197 °C. Found: C, 76.97; H, 7.89%. Calcd for $C_{27}H_{32}O_4$: C, 77.11; H, 7.67%. The IR and NMR spectra of **16** were identical with those of authentic royleanone benzoate.[2] Further elution with ether–benzene (1 : 9) afforded 12-benzoyloxy-11-methoxyabieta-8,11,13-trien-7-one (**15**) (2.731 g: 44%) which was recrystallized from methanol: mp 163—163.5 °C; $[\alpha]_D$+38.0°; IR: 1740, 1678, 1600 cm^{-1}; NMR: 0.99 (6H, s, $-\dot{C}(CH_3)_2$), 1.22 and 1.27 (each 3H, d, and J=7 Hz, $-CH(C\underline{H}_3)_2$), 1.40 (3H, s, $C_{10}-CH_3$), 3.70(3H, s, $-OCH_3$), 7.76 (1H, s, $C_{14}-H$), 7.3—8.4 (5H, m, aromatic protons). Found: C, 77.57; H, 7.83%. Calcd for $C_{28}H_{34}O_4$: C, 77.39; H, 7.89%.

7β-Acetoxy-12-benzoyloxy-11-methoxyabieta-8,11,13-triene (17) and Its 7α-Acetoxy Isomer (18). From the Methyl Ether (9): A mixture of **9** (1.00 g) and lead tetraacetate (3.00 g) in acetic acid (30 ml) was refluxed for 40 min with stirring in a stream of nitrogen. The mixture was cooled to room temperature and ethylene glycol (1.0 ml) was added. The mixture was further stirred at room temperature for 30 min, poured into water, and extracted with ether. The ether extract was washed successively with water, aqueous sodium hydrogencarbonate, and brine. After drying over sodium sulfate, the solvent was evaporated *in vacuo*. The residue was chromatographed on silica gel (120 g) using ether–benzene (2 : 98) as the eluent to give a mixture of **17** and **18** (647 mg: 57%) whose NMR spectrum showed the presence of **17** and **18** in a ratio of *ca.* 1 : 2 from the intensities of the C-14 proton signals. The crystallization of the mixture from methanol gave **18** (290 mg): mp 176—177 °C; $[\alpha]_D$+75.2°; IR: 1735 sh, 1725 cm^{-1}; NMR: 0.94 (6H, s, $-\dot{C}(CH_3)_2$), 1.19 and 1.21 (each 3H, d, and J=7 Hz, $-CH(C\underline{H}_3)_2$), 1.28 (3H, s, $C_{10}-CH_3$), 2.04 (3H, s, $-OCOCH_3$), 3.72 (3H, s, $-OCH_3$), 5.86 (1H, m, $W_{1/2}$=5 Hz, $C_{7\beta}-H$), 6.88 (1H, s, $C_{14}-H$), 7.3—8.4 (5H, m, aromatic protons). Found: C, 75.15; H, 7.94%. Calcd for $C_{30}H_{38}O_5$: C, 75.28; H, 8.00%.

The isolation of the pure 7β-acetate (**17**) was difficult; it showed the following NMR spectrum: 0.95 and 1.00 (each 3H and s, $-\dot{C}(CH_3)_2$), 1.18 (6H, bd, J=7 Hz, $-CH(C\underline{H}_3)_2$), 1.37(3H, s, $C_{10}-CH_3$), 2.09 (3H, s, $-OCOCH_3$), 3.70 (3H, s, $-OCH_3$), 5.93 (1H, m, $W_{1/2}$=15 Hz, $C_{7\alpha}-H$), 6.85 (1H, s, $C_{14}-H$), 7.3—8.4 (5H, m, aromatic protons).

From the Ketone (15): Sodium borohydride (600 mg) was added at 0—5 °C to a stirred solution of **15** (1.469 g) in methanol (20 ml). The mixture was further stirred at this temperature for 3 h, acidified with dilute hydrochloric acid, and extracted with ether. The ether extract was washed with brine, dried over sodium sulfate, and then evaporated *in vacuo* to give a mixture of alcohols (1.17 g). IR: 3590, 3350, 1740 cm^{-1}; NMR: 0.95 (6H, s, $-\dot{C}(CH_3)_2$), 1.28 (6H, d, J=7 Hz, $-CH(C\underline{H}_3)_2$), 1.33 (3H, s, $C_{10}-CH_3$), 3.70 (3H, s, $-OCH_3$), 4.3—4.8 (1H, m, C_7-H), 7.25 (1H, s, $C_{14}-H$), 7.3—8.3 (5H, m, aromatic protons).

An aliquot of the above mixture (880 mg) was dissolved in acetic anhydride (15 ml) and pyridine (1.5 ml), allowed to stand at room temperature for 24 h, and then diluted with ether. The ether solution was washed successively with dilute hydrochloric acid and water, dried over sodium sulfate, and evaporated *in vacuo* to give an oil (861 mg) whose NMR spectrum showed the presence of **17** and **18** in a ratio of *ca.* 5 : 1.

Oxidation of the 7α-Acetate (18). Chromium trioxide (900 mg) was added to a stirred solution of **18** (900 mg) in acetic acid (15 ml). The mixture was further stirred at room temperature for 20 h, poured into water, and extracted with ether. The ether extract was washed successively with water, aqueous sodium hydrogencarbonate, and water. After drying over sodium sulfate, the solvent was evaporated *in vacuo*. The residue was recrystallized from methanol to give 7α-acetoxy-12-benzoyloxyabieta-8,12-diene-11,14-dione (**21**)[16] (210 mg: 23%). Mp 261—262 °C; $[\alpha]_D$+42.0°; IR: 1738, 1664, 1655 sh cm^{-1}; MNR ($CDCl_3$): 0.89 (6H, s, $-\dot{C}(CH_3)_2$), 1.23 (6H, d, J=7 Hz, $-CH(C\underline{H}_3)_2$), 1.28 (3H, s, $C_{10}-CH_3$), 2.06 (3H, s, $-OCOCH_3$), 5.99 (1H, m, $W_{1/2}$=5 Hz, $C_{7\beta}-H$), 7.4—8.3 (5H, m, aromatic protons). The mother liquor of crystallization was evaporated *in vacuo* and the residue was chromatographed on silica gel (40 g) using ether–benzene (1 : 99) as the eluent to give **15** (354 mg).

Oxidation of the 7β-Acetate (17). A solution of **17** (900 mg) containing a small amount of **18** was oxidized with chromium trioxide (900 mg) at room temperature for 20 h. After the same work-up as described for the preparation of **21**, the crude product was recrystallized from methanol to afford **21** (40 mg). The mother liquor of crystallization was evaporated *in vacuo* and the residue was chromatographed on silica gel (40 g) using ether–benzene (1 : 99) as the eluent to give a quinone fraction (400 mg) which was recrystallized from methanol to give 7β-acetoxy-12-benzoyloxyabieta-8,12-diene-11,14-dione (**19**)[16] (140 mg). Mp 125—127 °C and 155—160 °C; $[\alpha]_D$+30.0°; IR: 1737, 1663, 1653 sh cm^{-1}; NMR ($CDCl_3$): 0.90 and 0.94 (each 3H and s, $-\dot{C}(CH_3)_2$), 1.20 and 1.26 (each 3H, d, and J= 7 Hz, $-CH(C\underline{H}_3)_2$), 1.39 (3H, s, $C_{10}-CH_3$), 2.08 (3H, s, $-OCOCH_3$), 6.02 (1H, t, J=8.5 Hz, $W_{1/2}$=17 Hz, $C_{7\alpha}-H$),

7.4—8.4 (5H, m, aromatic protons). Further elution gave **15** (68 mg). The mother liquor of the above crystallization was chromatographed on silica gel to afford some additional **15** (201 mg).

*Taxoquinone (**1**).* A mixture of **19** (103 mg) and 10% aqueous sodium hydroxide (4.0 ml) in methanol (15 ml) was refluxed for 30 min. After the addition of methanol (5.0 ml) and 10% hydrochloric acid (8.0 ml), the mixture was further refluxed for 5 min, cooled to room temperature, and extracted with ether. The ether extract was washed successively with water, aqueous sodium hydrogencarbonate, and brine, dried over sodium sulfate, and then evaporated *in vacuo*. The residue was chromatographed on silica gel (20 g) using ether–benzene (2 : 98) as the eluent to give taxoquinone (**1**) (49 mg: 68%) which was recrystallized from ether: mp 206—207 °C; $[\alpha]_D$+344° (lit,[4] mp 212—214 °C, $[\alpha]_D$+340°); IR: 3548, 3378, 1671, 1647, 1623, 1597 cm^{-1}; NMR ($CDCl_3$): 0.93 (6H, s, $-\dot{C}(CH_3)_2$), 1.22 (6H, d, J=7 Hz, $-CH(C\underline{H}_3)_2$), 1.35 (3H, s, C_{10}–CH_3), 3.84 (1H, d, J=2 Hz, $C_{7\beta}$–OH), 4.84 (1H, m, $W_{1/2}$=20 Hz, $C_{7\alpha}$–H), 7.33 (1H, s, C_{12}–OH). Found: C, 72.04; H, 8.60%. Calcd for $C_{20}H_{28}O_4$: C, 72.26; H, 8.49%. The synthetic **1** was shown to be identical with natural taxoquinone by mixed melting point determination and IR and NMR spectral comparisons.

*Dehydroroyleanone (**3**).* A mixture of **1** (36.1 mg) and *p*-toluenesulfonic acid (40 mg) in dry benzene (10 ml) was refluxed for 30 min. The mixture was cooled to room temperature, stirred with sodium hydrogencarbonate for 30 min, and then filtered. The filtrate was evaporated *in vacuo* and the residue was chromatographed on silica gel (15 g) using ether–benzene (2 : 98) as the eluent to give dehydroroyleanone (**3**) (12.5 mg: 37%) which was recrystallized from petroleum ether: mp 166—167 °C; $[\alpha]_D$−609° (lit,[6] mp 166—168.5 °C, $[\alpha]_D$−620°); IR: 3363, 1665, 1635, 1610 cm^{-1}; UV λ_{max} nm (ε): 247sh (8600), 333 (7100), 459 (610); NMR ($CDCl_3$): 0.98, 1.02, and 1.04 (each 3H and s, $-\dot{C}(CH_3)_2$ and C_{10}–CH_3), 1.22 (6H, d, J=7 Hz, $-CH(C\underline{H}_3)_2$), 2.14 (1H, t, J=3 Hz, C_5–H), 6.45 (1H, dd, J=3 and 10 Hz, C_6–H), 6.81 (1H, dd, J=3 and 10 Hz, C_7–H), 7.32 (1H, s, C_{12}–OH). Found: C, 76.52; H, 8.52%. Calcd for $C_{20}H_{26}O_3$: C, 76.40; H, 8.34%. The IR and NMR spectra of **3** were identical with those of natural dehydroroyleanone.

Further elution gave the recovered **1** (20.0 mg).

*7α-Acetoxyroyleanone (**2**).* A mixture of **21** (41.9 mg) in methanol (30 ml) and 5% aqueous sodium hydrogencarbonate (4.0 ml) was refluxed for 45 min and evaporated *in vacuo*. The residue was acidified with dilute hydrochloric acid, refluxed for 5 min, cooled to room temperature, and then extracted with ether. The ether extract was washed successively with aqueous sodium hydrogencarbonate and water, dried over sodium sulfate, and evaporated *in vacuo*. The residue (31.8 mg) was recrystallized from ethanol to give 7α-acetoxyroyleanone (**2**) (11.9 mg: 36%). Mp 212—214 °C; $[\alpha]_D$−7° (lit,[6] mp 212—214.5 °C, $[\alpha]_D$−14°); IR: 3390, 1736, 1671, 1642, 1608 cm^{-1}; UV λ_{max} nm (ε): 272 (12,400), 410 (760); NMR ($CDCl_3$): 0.84 (6H, s, $-\dot{C}(CH_3)_2$), 1.19 and 1.22 (each 3H, d, and J=7 Hz, $-CH(C\underline{H}_3)_2$), 1.24 (3H, s, C_{10}–CH_3), 2.02 (3H, s, $-OCOCH_3$), 5.94 (1H, m, $W_{1/2}$=6 Hz, $C_{7\beta}$–H), 7.13 (1H, s, C_{12}–OH). Found: C, 70.75; H, 8.23%. Calcd for $C_{22}H_{30}O_5$: C, 70.56; H, 8.08%. The synthetic **2** was shown to be identical with natural 7α-acetoxyroyleanone by mixed melting point determination and IR and NMR spectral comparisons.

*Horminone (**4**).* A mixture of **21** (105 mg) and 10% aqueous sodium hydroxide (4.0 ml) in methanol (20 ml) was refluxed for 30 min, acidified with 10% hydrochloric acid, and further refluxed for 5 min. After the same work-up as described for the preparation of **1**, the crude product (88.3 mg) was recrystallized from ether–petroleum ether to give horminone (**4**) (39.3 mg: 54%). Mp 176—178 °C; $[\alpha]_D$−120° (lit,[6] mp 172.5—174.5 °C, $[\alpha]_D$−132°); IR: 3570, 3380, 1671, 1647, 1627, 1601 cm^{-1}; NMR ($CDCl_3$): 0.91 and 0.99 (each 3H and s, $-\dot{C}(CH_3)_2$), 1.22 (3H, s, C_{10}–CH_3), 1.22 (6H, d, J=7 Hz, $-CH(C\underline{H}_3)_2$), 4.75 (1H, m, $W_{1/2}$=9 Hz, $C_{7\beta}$–H), 3.05 and 7.27 (each 1H and s, 2-OH). Found: C, 72.11; H, 8.38%. Calcd for $C_{20}H_{28}O_4$: C, 72.26; H, 8.49%. The synthetic **4** was shown to be identical with natural horminone by mixed melting point determination and IR and NMR spectral comparisons.

*7-Oxoroyleanone (**5**).* According to the method of Eugster *et al.*,[5] a mixture of **4** (160 mg) and active manganese dioxide (1.80 g) in dioxane (25 ml) was stirred at 75—80 °C for 44 h. The crude product was chromatographed on silica gel (20 g) using ether–benzene (3 : 97) as the eluent to give the recovered **4** (107 mg). Further elution with ether–benzene (1 : 9) afforded 7-oxoroyleanone (**5**) (13.0 mg) which was recrystallized from methanol: mp 202—203 °C dec (lit,[7] mp 204—205 °C); IR: 3400, 1695, 1663, 1645, 1575 cm^{-1}; NMR ($CDCl_3$): 0.93 and 0.96 (each 3H and s, $-\dot{C}(CH_3)_2$), 1.22 (6H, d, J=7 Hz, $-CH(C\underline{H}_3)_2$), 1.36 (3H, s, C_{10}–CH_3), 6.98 (1H, s, C_{12}–OH). The IR and NMR spectra of **5** were identical with those of natural 7-oxoroyleanone.

*12-Methoxyabieta-8,12-diene-7,11,14-trione (**22**).* A solution of **1** (110 mg) in ether was methylated at 0—5 °C with diazomethane to give 7β-hydroxy-12-methoxyabieta-8,12-diene-11,14-dione (**20**) (110 mg). The crude ether (**20**) was dissolved in pyridine (2.0 ml) and chromium trioxide (120 mg) was added at 0—5 °C. The mixture was stirred at room temperature for 45 h, poured into dilute hydrochloric acid, and extracted with ether. The ether extract was washed with brine, dried over sodium sulfate, and then evaporated *in vacuo*. The residue was chromatographed on silica gel (20 g) using ether–benzene (3 : 97) as the eluent to give **22** (26 mg) which was recrystallized from petroleum ether: mp 90—92 °C (lit,[7] mp 88—91 °C); IR: 1700, 1663, 1625, 1577 cm^{-1}; NMR ($CDCl_3$): 0.92 and 0.96 (each 3H and s, $-\dot{C}(CH_3)_2$), 1.19 and 1.21 (each 3H, d, and J=7 Hz, $-CH(C\underline{H}_3)_2$), 1.42 (3H, s, C_{10}–CH_3), 3.90 (3H, s, $-OCH_3$).

*Inuroyleanol (**6**).* A solution of sodium dithionite (300 mg) in water (1.0 ml) was added at 95—100 °C to a solution of **22** (42.0 mg) in acetic acid (1.5 ml). The mixture was stirred at this temperature for *ca.* 2 min, cooled to room temperature, and extracted with ether. The ether extract was washed successively with water, aqueous sodium hydrogencarbonate, and brine. After drying over sodium sulfate, the solvent was evaporated *in vacuo* and the residue was recrystallized from methanol to give inuroylcanol (**6**) (29.4 mg: 70%). Mp 185—186 °C; $[\alpha]_D$+106° (lit,[7] mp 185—187 °C, $[\alpha]_D$+113.9°); IR: 3520, 1620 cm^{-1}; NMR ($CDCl_3$): 0.96 (6H, s, $-\dot{C}(CH_3)_2$), 1.37 (3H, s, C_{10}–CH_3), 1.39 (6H, d, J=7 Hz, $-CH(C\underline{H}_3)_2$), 3.80 (3H, s, $-OCH_3$), 5.72 (1H, s, C_{11}–OH), 13.30 (1H, s, C_{14}–OH). Found: C, 72.77; H, 8.85%. Calcd for $C_{21}H_{30}O_4$: C, 72.80; H, 8.73%.

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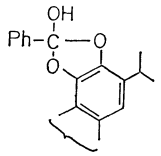
13) The methyl ether **10** should be produced by methylation of an intermediate (**8a**).



8a

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