A Convenient Synthesis of (±)-Taxodione, (±)-Ferruginol, and (±)-Sugiol

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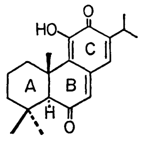
The condensation of β-cyclocitral (**4**) with 3-isopropyl-4-methoxybenzyl chloride (**5**) in the presence of lithium naphthalenide gave an alcohol (**6**), which was then oxidized to the corresponding α,β-unsaturated ketone (**7**). The Intramolecular cyclization of **7** with polyphosphoric acid yielded (±)-12-methoxyabieta-8,11,13-trien-6-one (**8**) and its *cis*-isomer (**9**), which was then successfully converted into **8** *via* an enol acetate (**11**). The **8** ketone was demethylated with boron tribromide to give a phenol (**18**), and this was then reduced with lithium aluminium hydride to yield the corresponding alcohol (**19**). The oxidation of the C-11 position in **19** with benzoyl peroxide gave (±)-12-benzoyloxyabieta-8,11,13-trien-6β,11-diol (**20**), which, on reduction with lithium aluminium hydride and subsequent oxidation with Jones reagent, afforded (±)-taxodione (**1**). The reductive cleavage of the hydroxyl group in **6** with dichloroaluminium hydride, followed by cyclization, gave (±)-ferruginyl methyl ether (**12**), which was then demethylated with boron tribromide to produce (±)-ferruginol (**2**). Further, the oxidation of **12** with chromium trioxide, followed by demethylation, gave (±)-sugiol (**3**).

Taxodione (**1**), a tumor-inhibitory diterpene quinone methide, was isolated from Taxodium distichum Rich by Kupchan *et al.*[1] In a previous paper, Matsumoto *et al.*[2] reported the total synthesis of (±)-**1** by the route of C→B→A ring construction. However, this synthetic route involves eighteen reaction steps and affords a low over-all yield (*ca.* 0.3%). Very recently, Matsumoto and Harada[3] also reported the syntheses of highly-oxygenated tricyclic diterpenes, taxoquinone, 7α-acetoxyroyleanone, dehydroroyleanone, horminone, 7-oxoroyleanone, and inuroyleanol, all starting from ferruginol (**2**). In conjunction with these previous works, we studied a general synthetic route for the naturally-occurring tricyclic diterpenes (C_{20} unit). This paper[4] will describe the simple and short-step syntheses of (±)-**1**, (±)-**2**, and (±)-sugiol (**3**) starting from two C_{10} units, β-cyclocitral (**4**)[5] and 3-isopropyl-4-methoxybenzyl chloride (**5**).

The condensation of **4** with **5** in the presence of lithium naphthalenide in tetrahydrofuran in a stream of nitrogen afforded the desired alcohol (**6**), which was then oxidized with the chromium trioxide–pyridine complex to yield an α,β-unsaturated ketone (**7**). The intramolecular cyclization of **7** with polyphosphoric acid afforded (±)-12-methoxyabieta-8,11,13-trien-6-one (**8**) as the minor product and its *cis*-isomer (**9**) as the major one, along with a small amount of (±)-xanthoperyl methyl ether (**10**),[6] which must have been produced by the air-oxidation of **9** during chromatographic purification. The *cis*-configuration of an A/B ring junction in **9** and **10** was supported by their NMR spectra, which showed signals due to the $C_{4\alpha}$ methyl group[7] at δ 0.32 and 0.44 ppm respectively. Since all natural compounds (**1**, **2**, and **3**) possess a *trans* A/B ring junction, the **9** *cis*-isomer was then converted into the **8** *trans*-isomer in the following manner. The oxidation of **9** with the Jones reagent readily produced **10**, which, on being refluxed with acetic anhydride in the presence of sodium acetate, gave the corresponding enol acetate (**11**) in a good yield. The **11** acetate in ethyl acetate was then submitted to catalytic hydrogenation over Pd–C in the presence of perchloric acid to afford a mixture of (±)-ferruginyl methyl ether (**12**, 33%), **8** (2%), (±)-6α- and (±)-6β-acetoxy-12-methoxyabieta-8,11,13-triene (**13**) (*ca.* 3:2, 42%), and (±)-12-methoxyabieta-8,11,13-trien-6α-ol (**14**, 5%). The treatment of **13** with lithium aluminium hydride in refluxing ether, followed by the oxidation of the resulting alcohols with the Jones reagent, afforded **8**. Further, the oxidation of **12** with lead tetraacetate in acetic acid afforded a mixture of 7α- and 7β-acetoxy compounds (**15**), which were then refluxed with dilute hydrochloric acid to yield (±)-12-methoxyabieta-6,8,11,13-tetraene (**16**). The **16** tetraene was then oxidized with *m*-chloroperoxybenzoic acid and the epoxide (**17**) was treated with dilute hydrochloric acid to give **8**. Subsequently, the **8** *trans*-ketone was demethylated with boron tribromide in dichloromethane, giving the corresponding phenol (**18**). The reduction of the carbonyl group in **18** was carried out with lithium aluminium hydride; (±)-abieta-8,11,13-trien-6β,12-diol (**19**) was thus obtained. The oxidation of the C-11 position in **19** with benzoyl peroxide in chloroform yielded (±)-12-benzoyloxy-abieta-8,11,13-trien-6β,11-diol (**20**), which responded positively to the Gibbs test,[8] suggesting the presence of an aromatic proton para to a phenolic hydroxyl group. The reductive cleavage of the benzoyl group in **20** with lithium aluminium hydride and the subsequent oxidation of the crude product with the Jones reagent afforded (±)-**1**. The IR and NMR spectra of the synthetic **1** were identical with those of natural taxodione. Thus, (±)-**1** was synthesized starting from β-cyclocitral (**4**) in eight steps, giving an over-all yield of *ca.* 7%.

As has been described above, ferruginol (**2**) is an important intermediate for the syntheses of the highly-oxygenated tricyclic diterpenes.[3] Therefore, it is worthwhile to synthesize **2** by a simple and short-step procedure, although several synthetic routes have already been reported by other workers.[9–13] For this purpose, the hydroxyl group in **6** was reductively removed with dichloroaluminium hydride in ether, and the resulting phenethyl derivative (**21**) was cyclized with anhydrous aluminium chloride in refluxing benzene, thus producing **12**. The demethylation of **12** with boron tribromide in dichloromethane gave (±)-ferruginol (**2**), which was characterized as its benzoate (**22**).[9,10,13] Subsequently, **12** was oxidized with chromium trioxide in acetic acid to afford the corresponding 7-oxo compound (**23**).[6] The demethylation of **23** with boron tribromide yielded (±)-sugiol (**3**),[11] which was also characterized as its acetate (**24**) and benzoate (**25**).



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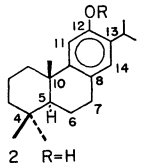
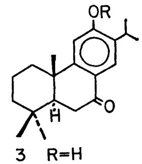
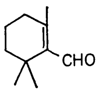


2 R=H
12 R=Me
22 R=COPh



3 R=H
23 R=Me
24 R=Ac
25 R=COPh



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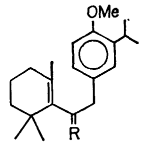
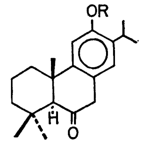
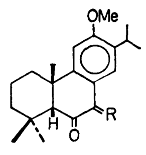


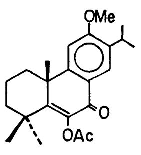
6 R=H, OH
7 R=O
21 R=H_2



8 R=Me
18 R=H



9 R=H_2
10 R=O



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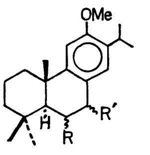
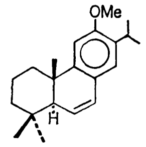


13 R=OAc, R′=H
14 R=OH, R′=H
15 R=H, R′=OAc



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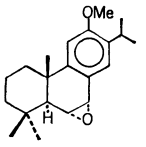

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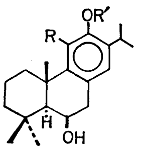

19 R=R′=H
20 R=OH, R′=COPh

Experimental

All melting points are uncorrected. The IR spectra were taken in chloroform, and the NMR spectra in carbon tetrachloride at 60 MHz, with tetramethylsilane as the internal standard, unless otherwise stated. The chemical shifts are presented in terms of δ values. Column chromatography was performed using Merck silica gel (0.063 mm).

3-Isopropyl-4-methoxybenzyl Chloride (5). A solution of methyl 3-isopropyl-4-methoxybenzoate (2.48 g)[14] in dry ether (7 ml) was added, drop by drop, to a suspension of lithium aluminium hydride (500 mg) in dry ether (20 ml) over a 20-min period. The mixture was then refluxed for 1 h, poured into an iced aqueous ammonium chloride solution, and extracted with ether. The extract was washed with brine. The dried extract was evaporated *in vacuo* to give 3-isopropyl-4-methoxybenzyl alcohol as an oil; NMR: 1.18 (d, 6, $J=7$ Hz, $-CH(C\underline{H}_3)_2$), 2.72 (s, 1, -OH), 3.28 (m, 1, $-C\underline{H}(CH_3)_2$), 3.78 (s, 3, $-OCH_3$), 4.42 (s, 2, $-CH_2-$), 6.65 (d, 1, $J=8$ Hz), 7.00 (dd, 1, $J=8$ and 2 Hz), and 7.07 (bs, 1) (aromatic protons).

A solution of the above alcohol in thionyl chloride (2.0 ml) was stirred at 0 °C for 30 min and then at room temperature for 1 h, decomposed with ice water, and extracted with ether. The dried extract was evaporated *in vacuo* to give **5** as an oil (1.82 g: 77%); NMR: 1.20 (d. 6, $J=7$ Hz, $-CH(C\underline{H}_3)_2$), 3.28 (m, 1, $-C\underline{H}(CH_3)_2$), 3.80 (s, 3, $-OCH_3$), 4.48 (s, 2, $-CH_2-$), 6.67 (d, 1, $J=9$ Hz), 7.08 (dd, 1, $J=9$ and 2 Hz), and 7.10 (d, 1, $J=2$ Hz) (aromatic protons).

In another experiment, the above benzyl alcohol derivative was prepared from 3-isopropyl-4-methoxybenzaldehyde[15] by a similar reduction.

Condensation of β-Cyclocitarl (4) and 3-Isopropyl-4-methoxybenzyl Chloride (5). A mixture of naphthalene (1.92 g) and small pieces of lithium (103 mg) in dry tetrahydrofuran (15 ml) was stirred for 1.5 h at room temperature under an atmosphere of nitrogen. Into the above solution we then stirred, drop by drop, a solution of β-cyclocitral (610 mg) and 3-isopropyl-4-methoxybenzyl chloride (890 mg) in dry tetrahydrofuran (3.0 ml) at 0—10 °C over a 15-min period. The mixture was then stirred at room temperature for 2.5 h in a stream of nitrogen, diluted with ether and then with aqueous ammonium chloride, and extracted with ether, and the extract was washed with brine. The dried extract was evaporated *in vacuo* to give a crude product which was subsequently purified by column chromatography on silica gel, using benzene–ether (98: 2) as the eluent, to afford an oily alcohol (**6**) (1.10 g: 87%); IR: 3580 cm^{-1}, NMR: 0.94 and 1.08 (each s, 6, $-\dot{C}(CH_3)_2$), 1.20 (d, 6, $J=7$ Hz, $-CH(C\underline{H}_3)_2$), 1.88 (s, 3, $=\dot{C}CH_3$), 3.15 (m, 1, $-C\underline{H}(CH_3)_2$), 3.77 (s, 3, $-OCH_3$), 4.27 (dd, 1, $J=4$ and 9 Hz, $-\dot{C}\underline{H}OH$), 6.63 (d, 1, $J=9$ Hz), 6.90 (dd, 1, $J=9$ and 2 Hz), and 6.92 (d, 1, $J=2$ Hz), (aromatic protons). Found: C, 79.93; H, 10.32%. Calcd for $C_{21}H_{32}O_2$: C, 79.70; H, 10.19%.

2,6,6-Trimethyl-1-cyclohexenyl 3-Isopropyl-4-methoxybenzyl Ketone (7). A solution of the **6** alcohol (5.424 g) in pyridine (10 ml) was added, drop by drop at 7—10 °C, to a chromium trioxide–pyridine complex prepared from chromium trioxide (5.0 g) and pyridine (50 ml). The mixture was stirred at 10—20 °C for 3.5 h, poured into ice-dilute hydrochloric acid, and extracted with ether. The ether extract was washed with brine, dried, and then evaporated. The crude product was purified by column chromatography on silica gel (500 g), using benzene–ether (99: 1) as the eluent, to give an α,β-unsaturated ketone **7** as an oil (3.507 g: 65%); IR: 1690 cm^{-1}, NMR: 1.02 (s, 6, $-\dot{C}(CH_3)_2$), 1.19 (d, 6, $J=7$ Hz, $-CH(C\underline{H}_3)_2$), 1.52 (s, 3, $=\dot{C}CH_3$), 3.29 (m, 1, $-C\underline{H}(CH_3)_2$), 3.65 (s, 2, $-COCH_2-$), 3.80 (s, 3, $-OCH_3$), 6.65 (d, 1, $J=8.5$ Hz), 6.91 (dd, 1, $J=8.5$ and 2 Hz), and 6.93 (d, 1, $J=2$ Hz) (aromatic protons). Found: C, 79.98; H, 9.43%. Calcd for $C_{21}H_{30}O_2$: C, 80.21; H, 9.62%.

Intramolecular Cyclization of 7. A mixture of **7** (879 mg) and polyphosphoric acid prepared, from 85% phosphoric acid (9 ml) and phosphorus pentaoxide (13 g) at 100 °C for 1 h, was heated at 100 °C for 1.5 h. After cooling, the mixture was diluted with water and extracted with ether, and the dried extract was evaporated to dryness. The crude product was purified by column chromatography on silica gel (90 g) using benzene–ether (99: 1 and then 97: 3) as the eluent, to give three ketones (**8**—**10**).

a) (±)-12-Methoxyabieta-8,11,13-trien-6-one (**8**) as an oil (182 mg: 21%); IR: 1708 cm^{-1}, NMR: 1.06 and 1.13 (each s, 6, $-\dot{C}(CH_3)_2$), 1.14 and 1.16 (each d and $J=7$ Hz, 6, $-CH(C\underline{H}_3)_2$), 1.28 (s, 3, $C_{10}-CH_3$), 2.29 (s, 1, C_5-H), 3.22 (m, 1, $-C\underline{H}(CH_3)_2$), 3.43 (s, 2, $-COCH_2-$), 3.78 (s, 3, $-OCH_3$) 6.67 and 6.75 (each s, 2, C_{11}-H and C_{14}-H). Found: C, 80.09; H, 9.32%. Calcd for $C_{21}H_{30}O_2$: C, 80.21; H, 9.62%

b) (±)-12-Methoxy-5βH-abieta-8,11,13-trien-6-one (**9**).

(341 mg: 39%); mp 94—95 °C (from methanol), IR: 1692 cm^{-1}, NMR: 0.33 (s, 3, $C_{4\alpha}$–CH_3), 0.92 (s, 3, $C_{4\beta}$–CH_3), 1.07 (s, 3, C_{10}–CH_3), 1.18 (d, 6, *J*=7 Hz, –CH($C\underline{H}_3$)$_2$), 1.99 (s, 1, C_5–H), 3.10 (m, 1, –C$\underline{H}$(CH_3)$_2$), 3.42 (s, 2, –$COCH_2$–), 3.83 (s, 3, –OCH_3), 6.70 and 6.78 (each s, 2, C_{11}–H and C_{14}–H). Found: C, 80.11; H, 9.54%. Calcd for $C_{21}H_{30}O_2$: C, 80.21; H, 9.62%.

c) (±)-Xanthoperyl methyl ether (**10**) (13 mg: 1%), which has been obtained from benzene–ether (97:3) fraction; mp 204—207 °C (from methanol) (lit,[6] mp 205 °C), IR: 1715, 1668 cm^{-1}, NMR ($CDCl_3$): 0.44 (s, 3, $C_{4\alpha}$–CH_3), 0.98 (s, 3, $C_{4\beta}$–CH_3), 1.23 (s, 3, C_{10}–CH_3), 1.24 (d, 6, *J*=7 Hz, –CH($C\underline{H}_3$)$_2$), 2.66 (s, 1, C_5–H), 3.28 (m, 1, –C$\underline{H}$(CH_3)$_2$), 3.98 (s, 3, –OCH_3), 6.82 (s, 1, C_{11}–H), 7.96 (s, 1, C_{14}–H). Found: C, 76.73; H, 8.69%. Calcd for $C_{21}H_{28}O_3$: C, 76.79; H, 8.59%.

The **10** diketone was also obtained in a 92% yield by the oxidation of **9** in acetone with the Jones reagent at room temperature for 30 min.

*(±)-6-Acetoxy-12-methoxyabieta-5,8,11,13-tetraen-7-one (**11**).* A mixture of **10** (511 mg) and anhydrous sodium acetate (2.0 g) in acetic anhydride (20 ml) was refluxed for 33 h, and then filtered. After the filtrate had been evaporated to dryness, the residue was extracted with ether and the extract was washed with aqueous sodium hydrogencarbonate and water. The dried extract was evaporated to yield a crude product which was subsequently purified by column chromatography on silica gel (70 g), using benzene–ether (97:3) as the eluent, to give **11** (556 mg: 96%), which was then recrystallized from methanol; mp 126—126.5 °C, IR: 1755, 1648 cm^{-1}, NMR: 1.22 and 1.26 (each d and *J*=7 Hz, 6, –CH($C\underline{H}_3$)$_2$), 1.31 and 1.36 (each s, 6, –$\overset{|}{C}$(CH_3)$_2$), 1.57 (s, 3, C_{10}–CH_3), 2.27 (s, 3, –$OCOCH_3$), 3.23 (m, 1, –C$\underline{H}$(CH_3)$_2$), 3.88 (s, 3, –OCH_3), 6.78 (s, 1, C_{11}–H), 7.79 (s, 1, C_{14}–H). Found: C, 74.70; H, 8.19%. Calcd for $C_{23}H_{30}O_4$: C, 74.56; H, 8.16%.

*Catalytic Hydrogenation of the Enol Acetate (**11**).* A mixture of **11** (283 mg), 5% Pd-C (250 mg), and 70% perchloric acid (10 drops) in ethyl acetate (10 ml) was subjected to catalytic hydrogenation at room temperature. After the usual work-up, the crude product was purified by column chromatography on silica gel (25 g), using hexane–benzene (1:1) and benzene–ether (97:3) as eluents, to yield **12**, **8**, **13**, and **14** (in the order of elution).

a) (±)-12-Methoxyabieta-8,11,13-triene (ferruginyl methyl ether) (**12**) as an oil (76 mg: 33%); NMR: 0.94 (s, 6, –$\overset{|}{C}$(CH_3)$_2$), 1.14 (d, 6, *J*=7 Hz, –CH($C\underline{H}_3$)$_2$), 1.18 (s, 3, C_{10}–CH_3), 3.15 (m, 1, –C$\underline{H}$(CH_3)$_2$), 3.72 (s, 3, –OCH_3), 6.53 and 6.67 (each s, 2, C_{11}–H and C_{14}–H). Found: C, 84.17; H, 10.76%. Calcd for $C_{21}H_{32}O$: C, 83.94; H, 10.73%.

b) **8** (4.3 mg: 2%), whose IR and NMR spectra were identical with those of (±)-12-methoxyabieta-8,11,13-trien-6-one.

c) (±)-6α- and 6β-Acetoxy-12-methoxyabieta-8,11,13-triene (**13**) as an oil (115 mg: 42%); IR: 1721 cm^{-1}. The ratio of 6α- and 6β-acetoxy compounds was found to be *ca.* 3:2 by NMR analysis of the mixture, using signals due to C_6–H at δ 5.35 (m, $W_{1/2}$=19 Hz) and 5.65 (m, $W_{1/2}$=10 Hz) ppm.

d) (±)-12-Methoxyabieta-8,11,13-trien-6α-ol (**14**) as an oil (13 mg: 5%); IR: 3600 cm^{-1}, NMR: 1.10, 1.10, and 1.15 (each s, 9, –$\overset{|}{C}$(CH_3)$_2$ and C_{10}–CH_3), 1.16 (d, 6, *J*=7 Hz, –CH($C\underline{H}_3$)$_2$), 4.20 (m, 1, $W_{1/2}$=16 Hz, C_6–H), 3.77 (s, 3, –OCH_3), 6.58 and 6.78 (each s, 2, C_{11}–H and C_{14}–H).

*(±)-12-Methoxyabieta-8,11,13-trien-6-one (**8**).* *a*) A mixture of **13** (177 mg) and lithium aluminium hydride (20 mg) in dry ether (10 ml) was refluxed for 1 h. After the usual work-up, the crude alcohol was immediately oxidized at 0 °C for 5 min with the Jones reagent (8N, 12 drops) in acetone (3.0 ml). The mixture was diluted with water, and the ether extract was washed with brine, dried, and evaporated. The product was then chromatographed on silica gel (15 g), using benzene as the eluent, to give a ketone (127 mg: 82%), whose IR and NMR spectra were identical with those of the *trans*-ketone **8**.

b) A solution of **12** (110 mg) and 85% lead tetraacetate (290 mg) in acetic acid (1.0 ml) was heated at 42—47 °C for 1 h in a stream of nitrogen. The solution was then diluted with water and extracted with ether, and the extract was washed successively with water, aqueous sodium hydrogencarbonate, and water. The dried extract was evaporated to give a crude acetate (**15**) (129 mg); IR: 1720 cm^{-1}, NMR: 1.97 and 2.06 (each s, C_7–$OCOCH_3$).

The above crude acetate (129 mg) was dissolved in ethanol (5.0 ml) containing 10% hydrochloric acid (1.0 ml) and refluxed for 2 h. After the solution had been diluted with ether, the ether solution was washed with brine, dried, and then evaporated to give (±)-12-methoxyabieta-6,8,11,13-tetraene (**16**) as an oil (109 mg); NMR: 0.97, 1.01, and 1.04 (each s, 9, –$\overset{|}{C}$(CH_3)$_2$ and C_{10}–CH_3), 1.15 and 1.19 (each d and *J*=7 Hz, 6, –CH($C\underline{H}_3$)$_2$), 3.21 (m, 1, –C$\underline{H}$(CH_3)$_2$, 3.79 (s, 3, –OCH_3), 5.78 (dd, 1, *J*=3 and 10 Hz, C_6–H), 6.42 (dd, 1, *J*=3 and 10 Hz, C_7–H), 6.57 and 6.77 (each s, 2, C_{11}–H and C_{14}–H).

A solution of **16** and 85% *m*-chloroperoxybenzoic acid (90 mg) in chloroform (3.0 ml) was allowed to stand at room temperature for 6 h and then diluted with ether. The solution was washed successively with aqueous potassium iodide, aqueous sodium hydrogencarbonate, and brine. After the removal of the solvent, the crude epoxide (**17**) was refluxed with dilute hydrochloric acid in ethanol (5.0 ml) for 1 h and then diluted with ether. The ether solution was washed with brine, dried, and evaporated. The chromatographic purification of the crude product afforded **8** (39 mg: 34% from **12**).

*(±)-12-Hydroxyabieta-8,11,13-trien-6-one (**18**).* A solution of **8** (143 mg) and boron tribromide (0.2 ml) in dichloromethane (2.0 ml) was stirred at 0 °C for 30 min, diluted with ether, and then poured into ice water. The mixture was extracted with ether, and the extract was washed successively with aqueous sodium thiosulfate and brine. The dried ether solution was then evaporated to dryness and purified by column chromatography on silica gel (15 g), using benzene–ether (97:3) as the eluent, to produce **18** (117 mg: 85%), which was subsequently recrystallized from hexane–acetone; mp 134—135 °C, IR: 3605, 3360, 1707 cm^{-1}, NMR: 1.08 and 1.10 (each s, 6, –$\overset{|}{C}$(CH_3)$_2$), 1.20 (d, 6, *J*=7 Hz, –CH($C\underline{H}_3$)$_2$), 1.29 (s, 3, C_{10}–CH_3), 2.33 (s, 1, C_5–H), 3.51 (s, 2, –$COCH_2$–), 6.15 (bs, 1, –OH), 6.67 and 6.73 (each s, 2, C_{11}–H and C_{14}–H). Found: C, 80.08; H, 9.34%. Calcd for $C_{20}H_{28}O_2$: C, 79.95; H, 9.39%.

*(±)-Abieta-8,11,13-trien-6β,12-diol (**19**).* A mixture of **18** (117 mg) and lithium aluminium hydride (20 mg) in dry ether (10 ml) was refluxed for 1 h. The mixture was then poured into ice-aqueous ammonium chloride and extracted with ether. The extract was washed with brine. The dried extract was evaporated to give **19** (108 mg: 92%), which was subsequently recrystallized from hexane–acetone; mp 174—176 °C, IR: 3610, 3350 cm^{-1}, NMR ($CDCl_3$): 1.03 and 1.28 (each s, 6, –$\overset{|}{C}$(CH_3)$_2$), 1.22 (d, 6, *J*=7 Hz, –CH($C\underline{H}_3$)$_2$), 1.53 (s, 3, C_{10}–CH_3), 4.5—4.9 (m, 2, –OH and C_6–H), 6.67 and 6.82 (each s, 2, C_{11}–H and C_{14}–H). Found: C, 79.24; H, 9.94%. Calcd for $C_{20}H_{30}O_2$: C, 79.42; H, 10.00%.

*(±)-12-Benzoyloxyabieta-8,11,13-trien-6β,11-diol (**20**).*

A solution of **19** (185 mg) and benzoyl peroxide (160 mg) in chloroform (10 ml) was allowed to stand at room temperature for 5 h, 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 removed and the residue was chromatographed on silica gel (35 g), using benzene–ether (98: 2) as the eluent, to yield **20** (152 mg: 59%), which responded positively to the Gibbs test;[8] mp 201—201.5 °C (from hexane–acetone), IR: 3580, 3400, 1743 cm^{-1}, NMR ($CDCl_3$): 1.04 and 1.23 (each s, 6, $-\overset{|}{C}(CH_3)_2$), 1.20 (d, 6, $J=7$ Hz, $-CH(C\underline{H}_3)_2$), 1.70 (s, 3, $C_{10}-CH_3$), 4.64 (m, 1, $W_{1/2}=9$ Hz, C_6-H), 6.62 (s, 1, $C_{14}-H$), 7.4—8.3 (m, 5, $-C_6H_5$). Found: C, 76.96; H, 8.20%. Calcd for $C_{27}H_{34}O_4$: C, 76.74; H, 8.11%.

(±)-Taxodione (1). A mixture of **20** (70.0 mg) and lithium aluminium hydride (30 mg) in dry tetrahydrofuran (10 ml) was refluxed for 1.5 h and then treated by a method similar to that used for **19**. The crude product was immediately oxidized with the Jones reagent (3 drops) in acetone (2.0 ml) at 0 °C for 2 min. After the usual work-up, the product was purified by column chromatography on silica gel (10 g), using hexane–benzene (1: 4) as the eluent, to yield an oil (**1**) (19.6 mg: 38%); IR: 3344, 1670, 1641, 1625, 1616, 1598 cm^{-1}, NMR: 1.10, 1.26, and 1.26 (each s, 9, $-\overset{|}{C}(CH_3)_2$ and $C_{10}-CH_3$), 1.18 (d, 6, $J=7$ Hz, $-CH(C\underline{H}_3)_2$), 2.50 (s, 1, C_5-H), 6.13 (s, 1, C_7-H), 6.85 (s, 1, $C_{14}-H$), 7.50 (s, 1, $-OH$). The IR and NMR spectra of (±)-**1** were identical with those of natural taxodione.

2-(2,6,6-Trimethyl-1-cyclohexenyl)-1-(3-isopropyl-4-methoxypheny)ethane (21). Lithium aluminium hydride (110 mg) was added to a solution of anhydrous aluminium chloride (1.2 g) in dry ether (18 ml), and then the mixture was stirred at room temperature for 100 min. To the above solution we then added, drop by drop, a solution of **6** (315 mg) in dry ether (4.0 ml) at 5—6 °C over an 8-min period. The mixture was further stirred at this temperature for 30 min, poured into ice-dilute hydrochloric acid, and extracted with ether. The ether extract was washed with brine, dried over sodium sulfate, and evaporated to give an oil which was purified by column chromatography on silica gel (30 g), using hexane as the eluent, to yield **21** (142 mg: 47%); NMR: 1.04 (s, 6, $-\overset{|}{C}(CH_3)_2$), 1.20 (d, 6, $J=7$ Hz, $-CH(CH_3)_2$), 1.65 (s, 3, $=\overset{|}{C}CH_3$), 3.23 (m, 1, $-C\underline{H}(CH_3)_2$), 3.74 (s, 3, $-OCH_3$), 6.58 (d, 1, $J=9$ Hz), 6.86 (dd, 1, $J=9$ and 3 Hz), and 6.9 (d, 1, $J=3$ Hz) (aromatic protons). Found: C, 84.14; H, 10.43%. Calcd for $C_{21}H_{32}O$: C, 83.94; H, 10.73%.

(±)-12-Methoxyabieta-8,11,13-triene (12). A mixture of **21** (298 mg), anhydrous aluminium chloride (140 mg), and dry benzene (10 ml) was refluxed for 3 h. The mixture was then poured into water and extracted with ether. The extract was washed with water, dried, and then evaporated. The chromatographic purification on silica gel (30 g) yielded **12** (155 mg: 52%), whose IR and NMR spectra were identical with those of an authentic sample.

(±)-Ferruginol (2). A solution of **12** (138 mg) and boron tribromide (0.2 ml) in dichloromethane (2.0 ml) was allowed to stand at room temperature for 2 h. The solution was then poured into water and extracted with ether. The extract was washed with brine, dried, and then evaporated to dryness. The crude product was purified by column chromatography on silica gel (15 g), using hexane–benzene (6: 4) as the eluent, to give **2** as an oil (127 mg: 96%); IR: 3605, 3355 cm^{-1}, NMR: 0.93 (s, 6, $-\overset{|}{C}(CH_3)_2$), 1.11 (s, 3, $C_{10}-CH_3$), 1.19 (d, 6, $J=7$ Hz, $-CH(C\underline{H}_3)_2$), 3.08 (m, 1, $-C\underline{H}(CH_3)_2$), 4.70 (s, 1, $-OH$), 6.42 and 6.67 (each s, 2, $C_{11}-H$ and $C_{14}-H$). The IR and NMR spectra of the synthetic **2** were identical with those of authentic ferruginol.

(±)-Ferruginyl Benzoate (22). A mixture of **2** (127 mg) and benzoyl chloride (0.1 ml) in pyridine (1.0 ml) was heated at 50 °C for 1 h. After the usual work-up, the crude product was chromatographed on silica gel (20 g), using benzene as the eluent, to yield **22** (146 mg: 85%), which was subsequently recrystallized from methanol; mp 125—126 °C (lit,[13] mp 127—130 °C), IR: 1728 cm^{-1}, NMR: 0.95 (s, 6, $-\overset{|}{C}(CH_3)_2$), 1.19 (d, 6, $J=7$ Hz, $-CH(C\underline{H}_3)_2$), 1.21 (s, 3, $C_{10}-CH_3$), 6.82 and 6.86 (each s, 2, $C_{11}-H$ and $C_{14}-H$), 7.3—8.2 (m, 5, $-C_6H_5$). Found: C, 83.01; H, 8.75%. Calcd for $C_{27}H_{34}O_2$: C, 83.03; H, 8.78%.

(±)-12-Methoxyabieta-8,11,13-trien-7-one (23). A mixture of **12** (161 mg) and chromium trioxide (160 mg) in acetic acid (5.0 ml) was stirred at room temperature for 11 h. After the usual work-up, the product was purified by column chromatography on silica gel (15 g), using benzene as the eluent, to yield **23** (110 mg: 65%), which was subsequently recrystallized from methanol; mp 125—126 °C (lit,[6] mp 125—126 °C), IR: 1660 cm^{-1}, NMR 0.95 and 1.00 (each s, 6, $-\overset{|}{C}(CH_3)_2$), 1.21 (d, 6, $J=7$ Hz, $-C\underline{H}(CH_3)_2$), 1.24 (s, 3, $C_{10}-CH_3$), 3.21 (m, 1, $-C\underline{H}(CH_3)_2$), 3.87 (s, 3, $-OCH_3$), 6.66 (s, 1, $C_{11}-H$), 7.69 (s, 1, $C_{14}-H$). Found: 80.01; H, 9.48%. Calcd for $C_{21}H_{30}O_2$: C, 80.21; H, 9.62%.

(±)-Sugiol (3). A solution of **23** (110 mg) and boron tribromide (0.3 ml) in dichloromethane (2.0 ml) was allowed to stand at room temperature for 4 h and then treated as has been described for **2**. The crude product was chromatographed on silica gel (15 g) and eluted with benzene–ether (99: 1) to give **3** (84 mg: 80%), which was then recrystallized from methanol; mp 246.5—247 °C, IR (KBr): 3120, 1643 cm^{-1}, NMR (pyridine-d_5): 0.83 and 0.87 (each s, 6, $-\overset{|}{C}(CH_3)_2$), 1.14 (s, 3, $C_{10}-CH_3$), 1.35 (d, 6, $J=7$ Hz, $-CH(C\underline{H}_3)_2$), 3.60 (m, 1, $-C\underline{H}(CH_3)_2$), 7.05 (s, 1, $C_{11}-H$), 8.30 (s, 1, $C_{14}-H$). Found: C, 79.73; H, 9.25%. Calcd for $C_{20}H_{28}O_2$: C, 79.95; H, 9.39%.

(±)-Sugiyl Acetate (24). A solution of **3** (49 mg) and acetic anhydride (0.2 ml) in pyridine (2.0 ml) was heated at 50—55 °C for 3 h. The crude product was then chromatographed on silica gel (10 g) and eluted with benzene to afford **24** as an oil (47 mg: 85%); IR: 1753, 1675 cm^{-1}, NMR ($CDCl_3$): 0.93 and 1.01 (each s, 6, $-\overset{|}{C}(CH_3)_2$), 1.22 (d, 6, $J=7$ Hz, $-CH(C\underline{H}_3)_2$), 1.25 (s, 3, $C_{10}-CH_3$), 2.32 (s, 3, $-OCOCH_3$), 2.99 (m, 1, $-C\underline{H}(CH_3)_2$), 6.96 (s, 1, $C_{11}-H$), 7.94 (s, 1, $C_{14}-H$). Found: C, 77.44; H, 8.88%. Calcd for $C_{22}H_{30}O_3$: C, 77.15; H, 8.83%. The NMR spectrum was identical with that published[7] for (+)-sugiyl acetate.

(±)-Sugiyl Benzoate (25). A solution of **3** (48 mg), benzoyl chloride (0.1 ml), and pyridine (1.0 ml) was heated at 50—55 °C for 1 h. The crude product was then chromatographed on silica gel (15 g) and eluted with benzene–ether (99: 1) to give **25** (57 mg: 88%), which was subsequently recrystallized from methanol; mp 164—166 °C, IR: 1734, 1673 cm^{-1}, NMR: 0.97 and 1.02 (each s, 6, $-\overset{|}{C}(CH_3)_2$), 1.25 and 1.27 (each d and $J=7$ Hz, 6, $-CH(C\underline{H}_3)_2$), 1.28 (s, 3, $C_{10}-CH_3$), 3.06 (m, 1, $-C\underline{H}(CH_3)_2$), 7.02 (s, 1, $C_{11}-H$), 7.89 (s, 1, $C_{14}-H$). Found: C, 80.05; H, 8.11%. Calcd for $C_{27}H_{32}O_3$: C, 80.16; H, 7.97%.

References

1) S. M. Kupchan, A. Karim, and C. Marcks, *J. Am. Chem. Soc.*, **90**, 5923 (1968); *J. Org. Chem.*, **34**, 3912 (1969).

2) T. Matsumoto, Y. Tachibana, J. Uchida, and K. Fukui, *Bull. Chem. Soc. Jpn.*, **44**, 2766 (1971).

3) T. Matsumoto and S. Harada, *Chem. Lett.*, **1976**, 1311.

4) Although the formulas depicted represent only one

enantiomer, they should be taken to indicate racemates.

5) R. N. Gedye, P. C. Arora, and K. Deck, *Can. J. Chem.*, **49**, 1764 (1971); W. M. Könst, L. M. van der Linde, and H. Boelens, *Tetrahedron Lett.*, **1974**, 3175.

6) D. Nasipuri and M. Guha, *J. Chem. Soc.*, **1962**, 4248.

7) Y. Kondo, T. Ikenoue, and T. Takemoto, *Chem. Pharm. Bull.*, **11**, 678 (1963).

8) F. E. King, T. J. King, and L. C. Manning, *J. Chem. Soc.*, **1957**, 563.

9) F. E. King, T. J. King, and J. G. Topliss, *J. Chem. Soc.*, **1957**, 573.

10) R. N. Rao and K. Raman, *Tetrahedron*, **4**, 294 (1958).

11) W. L. Meyer, G. B. Clemans, and R. W. Huffman, *Tetrahedron Lett.*, **1966**, 4255; W. L. Meyer, G. B. Clemans, and R. A. Manning, *J. Org. Chem.*, **40**, 3686 (1975).

12) M. Ohashi, T. Maruishi, and H. Kakisawa, *Tetrahedron Lett.*, **1968**, 719.

13) J. Wolinsky, R. Lau, J. J. Hamsher, and C. M. Cimarusti, *Synth. Commun.*, **2**, 327 (1972).

14) H. Gilman and N. O. Calloway, *J. Am. Chem. Soc*,. **55**, 4197 (1933).

15) H. Gilman and R. R. Burtner, *J. Am. Chem. Soc.*, **57**, 909 (1935).