The Synthesis of (+)-Pisiferol and (+)-Pisiferal

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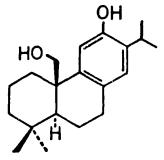
Reduction of abieta-8,11,13,-trien-6-one with lithium aluminium hydride, followed by treatment with lead tetraacetate and iodine, afforded 6*β*,20-epoxyabieta-8,11,13-triene. This was converted into a separable mixture of abieta-8,11,13-trien-20-ol (**13**) and 5*βH*-abieta-8,11,13-trien-20-ol (**14**) by a series of reactions; ether cleavage with acetic *p*-toluenesulfonic anhydride, catalytic hydrogenation, and reduction with lithium aluminium hydride. Acetylation of **13** and **14** gave the corresponding acetates, 20-acetoxyabieta-8,11,13-triene (**11**) and 20-acetoxy-5*βH*-abieta-8,11,13-triene (**12**). Friedel-Crafts acylation of **11** with acetyl chloride in the presence of anhydrous aluminium chloride afforded 20-acetoxy-12-acetylabieta-8,11,13-triene, which was converted into pisiferol by oxidation with *m*-chloroperbenzoic acid and subsequent treatment with lithium aluminium hydride. The synthetic pisiferol was oxidized with Jones reagent to give pisiferal. Similarly, 5*βH*-abieta-8,11,13-triene-12,20-diol was synthesized from **12**. Conversion of the cis A/B ring junctions in **12** into the trans ones is also described.

Pisiferol (**1**) and pisiferal (**2**), rare naturally-occurring tricyclic diterpenes possessing an oxidized angular methyl group, have recently been isolated from the leaves of *Chamaecyparis pisifera* (Cupressaceae) by Yatagai *et al.*[1,2] As a part of our synthetic studies on the naturally-occurring diterpenes, we have attempted the syntheses of these rare natural compounds. This paper will describe the syntheses of (+)-pisiferol (**1**) and (+)-pisiferal (**2**), starting from (+)-abieta-8,11,13-trien-6-one (**3**)[3-5] which was prepared from an epimeric mixture of 7*α*- and 7*β*-acetoxyabieta-8,11,13-triene (**4**)[3] in an improved yield.



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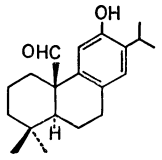

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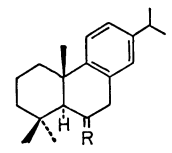
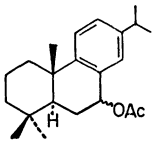
Treatment of the mixture **4** with 10% hydrochloric acid in refluxing ethanol afforded abieta-6,8,11,13-tetraene (**5**)[3-5] (84.4%). The tetraene **5** was oxidized at 0—5 °C with *m*-chloroperbenzoic acid in dichloromethane to give an epoxide (**6**) which, without purification, was converted into **3** (82.3% from **5**) by refluxing with *p*-toluenesulfonic acid in benzene. Reduction of **3** with lithium aluminium hydride in refluxing ether yielded abieta-8,11,13-trien-6*β*-ol (**7**: 87.3%). The stereochemistry of the hydroxyl group at C-6 in **7** was assigned to be *β*-configuration from its ^{1}H NMR spectrum, which showed a signal due to the angular methyl group at C-10 in a lower field (δ 1.51) than that of the corresponding signal (δ 1.29) in **3**. These down-field shift suggested a 1,3-diaxial *cis*-relationship between the angular methyl group and the hydroxyl group at C-6. In order to oxidize the angular methyl group by transannular oxidation, the alcohol **7** in benzene was treated with lead tetraacetate in the presence of iodine at room temperature under a stream of nitrogen. Purification of the crude product by column chromatography on silica gel afforded 6*β*,20-epoxyabieta-8,11,13-triene (**8**: 86.3%). The structure of **8** was supported by the appearance of signals due to methylene protons [ABq at δ 3.51 (d, J=8 Hz) and 3.82 (d, J=8 Hz)] in its ^{1}H NMR spectrum and by the disappearance of the signal due to the angular methyl group. Treatment of **8** with acetic *p*-toluenesulfonic anhydride[6] in dichloromethane at room temperature produced a mixture of 20-acetoxyabieta-5,8,11,13-tetraene (**9**) and 20-acetoxyabieta-6,8,11,13-tetraene (**10**) in 87.1% yield. The ^{1}H NMR spectrum of the mixture showed the presence of **9** [δ 3.33 (2H, d, J=4 Hz, C_7–H_2) and 6.17 (1H, t, J=4 Hz, C_6–H)] and **10** [δ 2.31 (1H, t, J=3 Hz, C_5–H), 5.97 (1H, dd, J=3 and 10 Hz, C_6–H), and 6.55 (1H, dd, J=3 and 10 Hz, C_7–H)] in a ratio of *ca.* 5:8. The mixture of **9** and **10** in acetic acid was submitted to catalytic hydrogenation over PtO_2 at room temperature to afford a mixture of 20-acetoxyabieta-8,11,13-triene (**11**) and its cis isomer (**12**). Because of the difficulty of the separation of **11** and **12**, the mixture was immediately treated with lithium aluminium hydride in refluxing ether. The repeated column chromatography of the crude product using silica gel afforded abieta-8,11,13-trien-20-ol (**13**) and its cis isomer (**14**) in 66.1% and 20.0% yields from the mixture of **9** and **10**. The *cis*-configuration of the A/B ring junction in **14** was supported by the appearance of a signal due to one of the *gem*-dimethyl groups at C-4 in very high field (δ 0.41) owing to the shielding effect of the aromatic C ring. Acetylation of **13** and **14** with acetic anhydride in pyridine gave the corresponding acetates, **11** (98.4%) and **12** (93.5%). The Friedel-Crafts acylation of **11** with acetyl chloride in dichloromethane in the presence of anhydrous aluminium chloride yielded 20-acetoxy-12-acetylabieta-8,11,13-triene (**15**: 85.4%), whose IR spectrum showed carbonyl bands at 1732 and 1680 cm^{-1}. The ^{1}H NMR spectrum of **15** showed two singlets at δ 6.94 and 7.30 due to the two aromatic protons. These spectral data of **15** supported the presence of an acetyl group at C-12. The Baeyer-Villiger oxidation of **15** with *m*-chloroperbenzoic acid in the presence of *p*-toluenesulfonic acid in refluxing 1,2-dichloroethane afforded 12,20-diacetoxyabieta-8,11,13-triene (**16**: 69.3%). Treatment of **16** with lithium aluminium hydride in refluxing ether yielded abieta-8,11,13-triene-12,20-diol (pisiferol) (**1**: 96.4%) which, on methylation with methyl iodide and anhydrous potassium carbonate in refluxing ethyl methyl ketone, afforded 12-methoxyabieta-8,11,13-trien-20-ol (**17**: 98.4%). The IR and

^{1}H NMR spectra of the synthetic **1** were identical with those of natural pisiferol. Oxidation[1] of **1** with Jones reagent at 0—5 °C afforded 12-hydroxyabieta-8,11,13-trien-20-al (pisiferal)[1,2] (**2**: 47.6%). Similarly, the cis acetate **12** was also converted into 5βH-abieta-8,11,13-triene-12,20-diol (**20**: 98.5%) *via* 20-acetoxy-12-acetyl-5βH-abieta-8,11,13-triene (**18**: 57.2%) and 12,20-diacetoxy-5βH-abieta-8,11,13-triene (**19**: 61.8%).



3 R=O
7 R=α-H, β-OH



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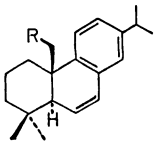
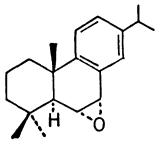


5 R=H
10 R=OAc



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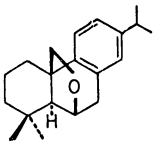

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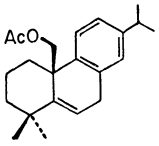
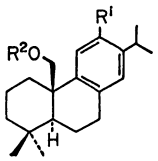
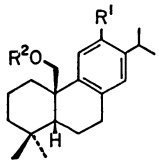


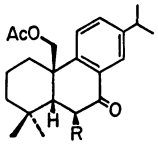
9



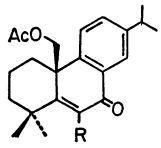
11 R^1=H, R^2=Ac
13 R^1=R^2=H
15 R^1=R^2=Ac
16 R^1=OAc, R^2=Ac
17 R^1=OMe, R^2=H



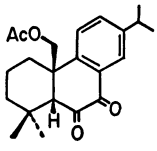
12 R^1=H, R^2=Ac
14 R^1=R^2=H
18 R^1=R^2=Ac
19 R^1=OAc, R^2=Ac
20 R^1=OH, R^2=H



21 R=H
23 R=Br



24 R=H
25 R=OAc



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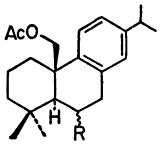

26 R=α-OAc
27 R=β-OAc

Subsequently, conversion of the cis A/B ring junctions into the trans ones was carried out as follows. The cis acetate **12** was oxidized with Jones reagent at room temperature to give 20-acetoxy-5βH-abieta-8,11,13-trien-7-one (**21**: 52.3%[7]) and 20-acetoxy-5βH-abieta-8,11,13-triene-6,7-dione (**22**: 28.8%[7]). Bromination of **21** with pyridinium tribromide in dichloromethane at room temperature afforded 20-acetoxy-6β-bromo-5βH-abieta-8,11,13-trien-7-one (**23**: 97.3%) which was converted into 20-acetoxyabieta-5,8,11,13-tetraen-7-one (**24**: 87.8%) by treatment with lithium carbonate and lithium bromide in *N*,*N*-dimethylformamide at 110—130 °C under a stream of nitrogen. The tetraene **24** in ethyl acetate was catalytically hydrogenated with 10% Pd–C in the presence of perchloric acid to give the trans acetate (**11**: 98.9%). The 6,7-dioxo acetate **22** was refluxed with anhydrous sodium acetate in acetic anhydride to give the corresponding enol acetate (**25**: 77.9%). The enol acetate **25** in ethyl acetate was then submitted to catalytic hydrogenation over 10% Pd–C in the presence of perchloric acid. Purification of the crude product by column chromatography on silica gel afforded **11** (28.8%) and a mixture (53.2%) of 6α,20- (**26**) and 6β,20-diacetoxyabieta-8,11,13-triene (**27**) (*ca.* 1:1 ratio).

Experimental

All melting points are uncorrected. The IR spectra and optical rotations were measured in chloroform and the ^{1}H NMR spectra 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, bs: broad singlet, d: doublet, bd: broad doublet, dd: double doublet, t: triplet, m: multiplet. The column chromatography was performed using Merck silica gel.

Abieta-6,8,11,13-tetraene (5). The epimeric mixture of 7α- and 7β-acetoxyabieta-8,11,13-triene (**4**)[3] was prepared from (+)-dehydroabietic acid.

A mixture of **4** (5.830 g) and dilute hydrochloric acid 10%: 8.5 ml) in ethanol (50 ml) was refluxed for 2.5 h and evaporated *in vacuo*. The residue was diluted with water and extracted with ether. The ether extract was washed with brine, dried over sodium sulfate, and evaporated *in vacuo*. The crude product was purified by column chromatography on silica gel (50 g), using hexane as the eluent, to give **5**[3-5] (4.023 g: 84.4%), $[\alpha]_D$ −124° (*c* 4.67).

Abieta-8,11,13-trien-6-one (3). A mixture of **5** (16.77 g) and *m*-chloroperbenzoic acid (80%: 17.50 g) in dichloromethane (170 ml) was stirred at 0—5 °C for 1.5 h. The mixture was diluted with ether and then washed successively with aqueous potassium iodide, aqueous sodium thiosulfate apueous sodium hydrogencarbonate, and brine. The solution was dried over sodium sulfate and evaporated *in vacuo* to give a crude epoxide (**6**) (17.38 g); ^{1}H NMR: 1.09, 1.14, and 1.20 (each 3H and s, $-\underset{|}{C}(CH_3)_2$ and C_{10}–CH_3), 1.26 (6H, d, J=7 Hz, $-CH(C\underline{H}_3)_2$), 2.83 (1H, m, $-C\underline{H}(CH_3)_2$), 3.29 (1H, t, J=4 Hz, $C_{6\beta}$–H), 3.61 (1H, d, J=4 Hz, $C_{7\beta}$–H), 6.98 (2H, bs, C_{11}–H and C_{12}–H), 7.24 (1H, bs, C_{14}–H).

A mixture of the crude epoxide **6** (17.38 g) and *p*-toluenesulfonic acid monohydrate (1.50 g) in dry benzene (250 ml) was refluxed for 1 h. The benzene solution was washed successively with water, aqueous sodium hydrogencarbonate, and brine. The solution was dried over sodium sulfate and evaporated *in vacuo*. The crude product was chromatographed on silica gel (300 g), using hexane–benzene (1:1) as the eluent, to give **3**[3-5] (14.63 g: 82.3% from **5**), $[\alpha]_D$ +125° (*c* 2.64), IR: 1710 cm^{-1}.

Abieta-8,11,13-trien-6β-ol (7). A mixture of **3** (3.196 g) and lithium aluminium hydride (420 mg) in dry ether (50 ml) was stirred at 0—5 °C for 5 min and then refluxed for 1.5 h. The mixture was poured into ice-dilute hydrochloric acid, and exteacted with ether. The ether extract was washed with brine, dried over sodium sulfate, and evaporated *in vacuo*. The residue was chromatographed on silica gel (150 g), using benzene as the eluent, to give **3** (89 mg: 2.8%). Further elution with the same solvent afforded **7** (2.808 g: 87.3%) as a solid, mp 100—101 °C, $[\alpha]_D$ +40.8° (*c* 5.15); IR: 3615, 3480 cm^{-1}; ^1H NMR: 0.99 and 1.23 (each 3H and s, $-\dot{C}(CH_3)_2$), 1.22 (6H, d, J=7 Hz, $-CH(C\underline{H}_3)_2$), 1.51 (3H, s, C_{10}-CH_3), 4.50 (1H, bs, $W_{1/2}$=9.5 Hz, $C_{6\alpha}$-H), 6.73 (1H, bs, C_{14}-H), 6.85 (1H, bd, J=8 Hz, C_{12}-H), 7.10 (1H, d, J=8 Hz, C_{11}-H). Found: C, 83.85; H, 10.75%. Calcd for $C_{20}H_{30}O$: C, 83.86; H, 10.56%.

6β,20-Epoxyabieta-8,11,13-triene (8). A mixture of **7** (13.18 g), lead tetraacetate (87.5%: 32.2 g), and iodine (16.6 g) in dry benzene (250 ml) was stirred for 2 h under a stream of nitrogen with cooling in a water bath. The mixture was diluted with benzene and the organic solution was washed successively with aqueous sodium thiosulfate, aqueous sodium hydrogencarbonate, and brine. The dried solution was evaporated *in vacuo*. The crude product was purified by column chromatography on silica gel (500 g), using benzene as the eluent, to give **8** (11.30 g: 86.3%), $[\alpha]_D$ −64.4° (*c* 2.10); ^1H NMR: 0.93 and 1.02 (each 3H and s, $-\dot{C}(CH_3)_2$), 1.20 (6H, d, J=7 Hz, $-CH(C\underline{H}_3)_2$), 2.76 (1H, m, $-C\underline{H}(CH_3)_2$), 2.92 (2H, bd, J=2.5 Hz, C_7-H_2), 3.51 and 3.82 (ABq, each 1H and d, J=8 Hz, $-CH_2O-$), 4.35 (1H, t, J=2.5 Hz, $-\dot{C}HO-$). Found: C, 84.53; H, 10.21%. Calcd for $C_{20}H_{28}O$: C, 84.45; H, 9.92%.

Ether Cleavage of 8. A mixture of **8** (8.131 g) and acetic *p*-toluenesulfonic anhydride (18.40 g) in dichloromethane (150 ml) was stirred at room temperature for 2.5 h and then diluted with ether. The ether solution was washed successively with aqueous sodium hydrogencarbonate and brine, dried over sodium sulfate, and evaporated *in vacuo*. The crude product was chromatographed on silica gel (500 g), using benzene as the eluent, to give a mixture (8.13 g: 87.1%) of 20-acetoxyabieta-5,8,11,13-tetraene (**9**) and 20-acetoxyabieta-6,8,11,13-tetraene (**10**) in a ratio of *ca.* 5:8 by ^1H NMR spectrum analysis. ^1H NMR of **9** ($CDCl_3$, 90 MHz): 1.85 (3H, s, $-OCOCH_3$), 3.33 (2H, d, J=4 Hz, $=CHC\underline{H}_2-$), 4.13 (2H, s, $-C\underline{H}_2OCOCH_3$), 6.17 (1H, t, J=4 Hz, C_6-H). ^1H NMR of **10** ($CDCl_3$, 90 MHz): 1.74 (3H, s, $-OCOCH_3$), 2.31 (1H, t, J=3 Hz, $C_{5\alpha}$-H), 4.23 and 4.38 (ABq, each 1H and d, J=11 Hz, $-C\underline{H}_2OCOCH_3$), 5.97 (1H, dd, J=3 and 10 Hz, C_6-H), 6.55 (1H, dd, J=3 and 10 Hz, C_7-H).

Abieta-8,11,13-trien-20-ol (13) and 5βH-Abieta-8,11-13-trien-20-ol (14). A mixture (9.180 g) of **9** and **10** in acetic acid (25 ml) was submitted to catalytic hydrogenation using PtO_2 (1.0 g) at room temperature.

The crude product (8.848 g) was immediately treated for 2 h with lithium aluminium hydride (2.04 g) in refluxing ether (100 ml). The excess lithium aluminium hydride was decomposed with ethyl acetate. The mixture was poured into ice-dilute hydrochloric acid and extracted with ether. The ether extract was washed with brine, dried over sodium sulfate, and evaporated *in vacuo*. The residue was purified by repeated column chromatography on silica gel, using ether–benzene (1:99) as the eluent, to give **13** (5.323 g: 66.1%) and **14** (1.614 g: 20.0%). Alcohol **13**: $[\alpha]_D$ +41.6° (*c* 4.93); IR: 3580, 3440 cm^{-1}; ^1H NMR: 0.97 (6H, s, $-\dot{C}(CH_3)_2$), 1.20 (6H, d, J=7 Hz, $-CH(C\underline{H}_3)_2$), 3.45 and 3.73 (ABq, each 1H and bd, J=11 Hz, $-C\underline{H}_2OH$). Found: C, 84.02; H, 10.61%. Calcd for $C_{20}H_{30}O$: C, 83.86; H, 10.56%. Alcohol **14**: $[\alpha]_D$ +17.4° (*c* 2.24); IR: 3610, 3580, 3430 cm^{-1}; ^1H NMR: 0.41 (3H, s, $C_{4\alpha}$-CH_3), 0.95 (3H, s, $C_{4\beta}$-CH_3), 1.21 (6H, d, J=7 Hz, $-CH(C\underline{H}_3)_2$), 3.27 (2H, bs, $-C\underline{H}_2OH$), 6.77 (1H, bs, C_{14}-H), 6.83 (1H, dd, J=1.5 and 8 Hz, C_{12}-H), 7.10 (1H, d, J=8 Hz, C_{11}-H). Found: C, 83.98; H, 10.70%. Calcd for $C_{20}H_{30}O$: C, 83.86; H, 10.56%.

20-Acetoxyabieta-8,11,13-triene (11). A mixture of **13** (885 mg) and acetic anhydride (1.0 ml) in pyridine (2.0 ml) was heated at 70—80 °C for 2 h. After the usual work-up, the crude product was chromatographed on silica gel (40 g), using benzene as the eluent, to give **11** (999 mg: 98.4%), $[\alpha]_D$ +56.0° (*c* 3.89), IR: 1733 cm^{-1}; ^1H NMR: 0.99 (6H, bs, $-\dot{C}(CH_3)_2$), 1.21 (6H, d, J=7 Hz, $-CH(C\underline{H}_3)_2$), 1.79 (3H, s, $-OCOCH_3$), 4.03 and 4.43 (ABq, each 1H and d, J=11 Hz, $-C\underline{H}_2OCOCH_3$). Found: C, 80.17; H, 10.01%. Calcd for $C_{22}H_{32}O_2$: C, 80.44; H, 9.83.

20-Acetoxy-5βH-abieta-8,11,13-triene (12). A mixture of **14** (403.1 mg) and acetic anhydride (0.5 ml) in pyridine (1.0 ml) was heated at 70—80 °C for 2 h. After the usual work-up, the crude product was chromatographed on silica gel (30 g), using ether–benzene (1:99) as the eluent, to give **12** (432.0 mg: 93.5%), $[\alpha]_D$ +29.0° (*c* 8.14), IR: 1726 cm^{-1}; ^1H NMR: 0.39 (3H, s, $C_{4\alpha}$-CH_3), 0.94 (3H, s, $C_{4\beta}$-CH_3), 1.21 (6H, d, J=7 Hz, $-CH(C\underline{H}_3)_2$), 1.93 (3H, s, $-OCOCH_3$), 3.63 and 3.97 (ABq, each 1H and d, J=11 Hz, $-C\underline{H}_2OCOCH_3$), 6.78 (1H, bs, C_{14}-H), 6.86 (1H, bd, J=8 Hz, C_{12}-H), 7.13 (1H, d, J=8 Hz, C_{11}-H). Found: C, 80.56; H, 10.13%. Calcd for $C_{22}H_{32}O_2$: C, 80.44; H, 9.83%.

20-Acetoxy-12-acetylabieta-8,11,13-triene (15). Anhydrous aluminium chloride (1.20 g) was added at 0—5 °C to a stirred solution of **11** (962.3 mg) and acetyl chloride (0.65 ml) in dichloromethane (16 ml). The mixture was stirred at this temperature for 5 min and then at room temperature for 3 h, poured into ice-dilute hydrochloric acid, and extracted with ether. The ether extract was washed successively with aqueous sodium hydrogencarbonate and brine, dried over sodium sulfate, and evaporated *in vacuo*. The residue was chromatographed on silica gel (60 g), using ether–benzene (3.97) as the eluent, to give **15** (927.8 mg: 85.4%), $[\alpha]_D$ +30.6° (*c* 13.02); IR: 1732, 1680 cm^{-1}; ^1H NMR: 0.99 (6H, s, $-\dot{C}(CH_3)_2$), 1.18 (6H, d, J=7 Hz, $-CH(C\underline{H}_3)_2$), 1.80 (3H, s, $-OCOCH_3$), 2.44 (3H, s, C_{12}-$COCH_3$), 3.45 (1H, m, $-C\underline{H}(CH_3)_2$), 4.01 and 4.47 (ABq, each 1H and d, J=11 Hz, $-C\underline{H}_2OCOCH_3$), 6.94 (1H, bs, C_{14}-H), 7.30 (1H, s, C_{11}-H). Found: C, 78.07; H, 9.39%. Calcd for $C_{24}H_{34}O_3$: C, 77.80;H, 9.25%.

12,20-Diacetoxyabieta-8,11,13-triene (16). A mixture of **15** (906.0 mg), *m*-chloroperbenzoic acid (80%: 1.05 g), and *p*-toluenesulfonic acid monohydrate (30 mg) in 1,2-dichloroethane (23 ml) was refluxed for 2 h. The mixture was cooled, diluted with ether, and washed successively with aqueous potassium iodide, aqueous sodium thiosulfate,

aqueous sodium hydrogencarbonate, and brine. The dried ether solution was evaporated *in vacuo*. The residue was chromatographed on silica gel (60 g), using ether–benzene (0.5:99.5) as the eluent, to give **16** (655.4 mg: 69.3%), $[\alpha]_D$ +51.9° (*c* 2.37·; IR: 1750 sh, 1732 cm^{-1}; ^1H NMR: 0.97 6H, s, $-C(CH_3)_2$), 1.15 (6H, d, J=7 Hz, $-CH(CH_3)_2$), 1.82 (3H, s, C_{20}-$OCOCH_3$), 2.21 (3H, s, C_{12}-$OCOCH_3$), 4.00 and 4.37 (ABq, each 1H and d, J=11 Hz, $-CH_2OCOCH_3$), 6.69 and 6.18 (each 1H and s, C_{11}-H and C_{14}-H). Found: C, 74.58; H, 8.95%. Calcd for $C_{24}H_{34}O_4$: C, 74.57; H, 8.87%.

*Abieta-8,11,13-triene-12,20-diol (Pisiferol) (**1**).* A mixture of **16** (495.7 mg) and lithium aluminium hydride (195 mg) in dry ether (5.0 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 brine, dried over sodium sulfate, and evaporated *in vacuo*. The crude product was purified by column chromatography on silica gel (25 g), using ether–benzene (7:93) as the eluent, to give **1** (373.9 mg: 96.4%), which was recrystallized from hexane, mp 147—148.5 °C, $[\alpha]_D$ +79.6° (*c* 2.21); IR: 3580, 3330 cm^{-1}; H^1 NMR ($CDCl_3$, 90 MHz): 0.90 and 0.94 (each 3H and s, $-C(CH_3)_2$), 1.22 (6H, d, J=7 Hz, $-CH(CH_3)_2$), 3.18 (1H, m, $-CH(CH_3)_2$), 3.57 and 3.98 (ABq, each 1H and d, J=11 Hz, $-CH_2OH$), 6.03 (1H, bs, -OH), 6.71 (1H, s) and 6.91 (1H, bs) (C_{11}-H and C_{14}-H). Found: C, 79.71; H, 10.19%. Calcd for $C_{20}H_{30}O_2$: C, 79.42; H, 10.00%. The IR and ^1H MNR spectra of the synthetic **1** were identical with those of natural pisiferol. However, the melting point of the synthetic **1** was higher than that reported (mp 108—110 °C) for natural pisiferol.[8]

*12-Hydroxyabieta-8,11,13-trien-20-al (Pisiferal) (**2**).* A solution of **1** (127.3 mg) in acetone (4.0 ml) was oxidized with Jones reagent [2.5 M (1 M=1 mol dm^{-3}): 0.2 ml] at 0—5°C for 1 min. The mixture was diluted with water and extracted with ether. The ether extract was washed with brine, dried over sodium sulfate, and evaporated *in vacuo*. The residue was chromatographed on silica gel (10 g), using ether–benzene (1:99) as the eluent, to give **2** (60.2 mg: 47.6%), which was recrystallized from hexane, mp 125.5—127 °C, $[\alpha]_D$ +386° (*c* 0.29); IR: 3595, 3360, 2745, 1700 cm^{-1}; ^1H NMR ($CDCl_3$, 90 MHz): 0.82 and 1.00 (each 3H and s, $-C(CH_3)_2$), 1.20 (6H, d, J=7 Hz, $-CH(CH_3)_2$), 2.92 (2H, *t*, J=6 Hz, C_7-H_2), 3.15 (1H, m, $-CH(CH_3)_2$), 5.63 (1H, bs, C_{12}-OH), 6.64 (1H, s) and 6.92 (1H, bs) (C_{11}-H and C_{14}-H), 9.90 (1H, d, J=1.5 Hz, -CHO); MS (*m/e*): 300 (M^+). The IR and ^1H NMR spectra of the synthetic **2** were identical with those of natural pisiferal. However, the melting point of the synthetic **2** was also higher than that reported (mp 80—82 °C[1]) for natural pisiferal.

*12-Methoxyabieta-8,11,13-trien-20-ol (**17**).* A stirred mixture of **1** (48.3 mg), methyl iodide (0.1 ml), and anhydrous potassium carbonate (220 mg) in ethyl methyl ketone (2.0 ml) was refluxed for 8 h. The mixture was diluted with water and extracted with ether. The ether extract was washed successively with aqueous sodium thiosulfate and brine, dried over sodium sulfate, and evaporated *in vacuo*. The residue was chromatographed on silica gel (5.0 g), using ether–benzene (2:98) as the eluent, to give **17** (49.6 mg: 98.4%), $[\alpha]_D$ +61.9° (*c* 0.70); IR: 3580, 3450 sh cm^{-1}; ^1H MNR: 0.97 (6H, s, $-C(CH_3)_2$), 1.16 (6H, d, J=7 Hz, $-CH(CH_3)_2$), 3.78 (3H, s, $-OCH_3$), 6.61 (1H, s) and 6.73 (1H, bs) (C_{11}-H and C_{14}-H). Found: C, 79.70; H, 10.47%. Calcd for $C_{21}H_{32}O_2$: C, 79.70; H, 10·19%.

*20-Acetoxy-12-acetyl-5β*H*-abieta-8,11,13-triene (**18**)* Anhydrous aluminium chloride (540 mg) was added at 0—5 °C to a stirred solution of **12** (428.3 mg) and acetyl chloride (0.29 ml) in dichloromethane (7.0 ml). The mixture was stirred at this temperature for 5 min and then at room temperature for 3 h. After the same work-up as described for the preparation of **15**, the crude product was purified by column chromatography on silica gel (20 g), using benzene and then ether–benzene (1:99) as the eluent, to give **18** (276.4 mg: 57.2%), $[\alpha]_D$ +18.8° (*c* 5.32); IR; 1733, 1680 cm^{-1}; ^1H NMR: 0.41 (3H, s, $C_{4\alpha}$-CH_3) 0.97 (3H, s, $C_{4\beta}$-CH_3), 1.20 (6H, d, J=7 Hz, $-CH(CH_3)_2$), 1.96 (3H, s, $-OCOCH_3$), 2.50 (3H, s, C_{12}-$COCH_3$), 3.70 and 3.97 (ABq, each 1H and d, J=11 Hz, $-CH_2OCOCH_3$), 6.98 (1H, bs, C_{14}-H), 7.40 (1H, s, C_{11}-H). Found: C, 77.65; H, 9.42%. Calcd for $C_{24}H_{31}O_3$: C, 77.80; H, 9.25%.

*16,20-Diacetoxy-5β*H*-abieta-8,11,13-triene (**19**)* A mixture of **18** (283.9 mg), *m*-chloroperbenzoic acid (80%: 330 mg), and *p*-toluenesulfonic acid monohydrate (5.0 mg) in 1,2-dichloroethane (6.0 ml) was refluxed for 2 h. After the same work-up as described for the preparation of **16**, the crude product was chromatographed on silica gel (50 g), using ether–benzene (1:99) as the eluent, to give **19** (185.8 mg: 61.8%), $[\alpha]_D$ +25.9° (*c* 3.13); IR: 1750 sh, 1732 cm^{-1}; ^1H NMR: 0.39 (3H, s, $C_{4\alpha}$-CH_3), 0.94 (3H, s, $C_{4\beta}$-CH_3), 1.17 (6H, d, J=7 Hz, $-CH(CH_3)_2$), 1.94 (3H, s, C_{20}-$OCOCH_3$), 2.24 (3H, s, C_{12}-$OCOCH_3$), 3.86 (2H, s, $-CH_2OCOCH_3$), 6.80 (1H, s) and 6.85 (1H, bs) (C_{11}-H and C_{14}-H). Found: C, 74.74; H, 9.11%. Calcd for $C_{24}H_{34}O_4$: C, 74.57; H, 8.87%.

*5β*H*-Abieta-8,11,13-triene-12,20-diol (**20**).* A mixture of **19** (153.3 mg) and lithium aluminium hydride (60 mg) in dry ether (5.0 ml) was refluxed for 2 h. After the same work-up as described for the preparation of **1**, the crude product was chromatographed on silica gel (10 g), using ether–benzene (8:92) as the eluent, to give **20** (125.7 mg: 98.5%). This was recrystallized from hexane, mp 113.5—115 °C, $[\alpha]_D$ +27.4° (*c* 2.60); IR: 3600, 3350 cm^{-1}; ^1H NMR ($CDCl_3$): 0.44 (3H, s, $C_{4\alpha}$-CH_3), 0.93 (3H, s, $C_{4\beta}$-CH_3), 1.22 (6H, d, J=7 Hz, $-CH(CH_3)_2$), 3.15 (1H, m, $-CH(CH_3)_2$), 3.38 (2H, bs, $-CH_2OH$), 6.65 (1H, s) and 6.79 (1H, bs) (C_{11}-H and C_{14}-H). Found: C, 79.37; H, 10.27%. Calcd for $C_{20}H_{30}O_2$: C, 79.42; H, 10.00%.

*Oxidation of **12**.* A solution of **12** (175.0 mg) in acetone (3.0 ml) was oxidized with Jones reagent (2.5 M: 0.3 ml) at room temperature for 2.5 h and then diluted with ether. The ether solution was washed with brine, dried over sodium sulfate, and evaporated *in vacuo*. The residue was chromatographed on silica gel (10 g), using benzene as the eluent, to give the starting **12** (79.7 mg: 45.5%). Subsequent elution with ether–benzene (3:97) afforded 20-acetoxy-5*βH*-abieta-8,11,13-trien-7-one (**21**) (52.0 mg: 28.5%; 52.3%[7]), $[\alpha]_D$ +40.0° (*c* 5.88); IR: 1735, 1672, 1608 cm^{-1}; ^1H NMR: 0.69 (3H, s, $C_{4\alpha}$-CH_3), 0.99 (6H, d, J=7 Hz, $-CH(CH_3)_2$), 1.05 (3H, s, $C_{4\beta}$-CH_3), 1.66 (3H, s, $-OCOCH_3$), 2.49 (2H, bd, J=5.5 Hz, $-CH_2CO-$), 2.64 (1H, m, $-CH(CH_3)_2$), 3.43 and 3.74 (ABq, each 1H and d, J=12 Hz, $-CH_2OCOCH_3$), 6.98 (2H, bs, C_{11}-H and C_{12}-H), 7.52 (1H, bs, C_{14}-H). Found: C, 77.31; H, 9.05%. Calcd for $C_{22}H_{30}O_3$: C, 77.15; H, 8.83%.

Further elution with the same solvent afforded 20-acetoxy-5*βH*-abieta-8,11,13-triene-6,7-dione (**22**) (29.8 mg: 15.7%; 28.8%[7]), $[\alpha]_D$ +50.2° (*c* 6.15); IR: 1748, 1727, 1688, 1608 cm^{-1}; ^1H NMR: 0.66 (3H, s, $C_{1\alpha}$-CH_3), 1.00 (6H, d, J=7 Hz, $-CH(CH_3)_2$), 1.06 (3H, s, $C_{4\beta}$-CH_3), 1.48 (3H, s, $-OCOCH_3$), 2.21 (1H, s, $C_{5\beta}$-H), 3.25 and 3.65 (ABq, each 1H and d, J=11 Hz, $-CH_2OCOCH_3$), 6.99 (1H, d, J=9 Hz C_{11}-H), 7.18 (1H, dd, J=1.5 and 9 Hz, C_{12}-H),

7.58 (1H, d, $J=1.5$ Hz, C_{14}-H); MS (*m/e*): 356 (M^+).

20-Acetoxy-6β-bromo-5βH-abieta-8,11,13-trien-7-one (23) A mixture of **21** (68.5 mg) and 80% pyridinium tribromide (80 mg) in dichloromethane (1.5 ml) was stirred at room temperature for 1 h. The mixture was diluted with water and extracted with ether. The ether extract was washed successively with aqueous sodium thiosulfate and water, dried over sodium sulfate, and evaporated *in vacuo*. The residue was chromatographed on silica gel (10 g), using ether-benzene (3:97) as the eluent, to give **23** (82.0 mg: 97.3%); IR: 1735, 1680, 1608 cm^{-1}; ^1H NMR: 0.26 (3H, s, $C_{4\alpha}$-CH_3), 1.13 (3H, s, $C_{4\beta}$-CH_3), 1.29 (6H, d, $J=7$ Hz, -CH($C\underline{H}_3$)$_2$), 1.99 (3H, s, -OCOCH_3), 2.61 (1H, s, $C_{5\beta}$-H), 2.94 (1H, m, -$C\underline{H}$(CH_3)$_2$), 3.81 and 4.12 (ABq, each 1H and d, $J=11.5$ Hz, -$C\underline{H}_2$OCOCH_3), 4.72 (1H, s, $C_{6\alpha}$-H), 7.15—7.5 (2H, m, C_{11}-H and C_{12}-H), 7.77 (1H, bs, C_{14}-H); MS (*m/e*): 422 (M^++2), 420 (M^+),

20-Acetoxyabieta-5,8,11,13-tetraen-7-one (24). A mixture of **23** (364.0 mg), lithium carbonate (192 mg), and lithium bromide (150 mg) in *N*,*N*-dimethylformamide (4.5 ml) was stirred at 110—130 °C for 4 h under a stream of nitrogen. The mixture was cooled, poured into ice-dilute hydrochloric acid, and extraced with ether. The ether extract was washed successively with aqueous sodium thiosulfate and brine, dried over sodium sulfate, and evaporated *in vacuo*. The crude product was purified by column chromatography on silica gel (20 g), using ether-benzene (3:97) as the eluent, to give **24** (258.3 mg: 87.8%). This was recrystallized from hexane, mp 75—76 °C, $[\alpha]_D$ −17.5° (*c* 5.15); IR: 1735, 1650, 1608 cm^{-1}; ^1H NMR: 1.28 (6H, d, $J=7$ Hz, -CH($C\underline{H}_3$)$_2$), 1.30 (6H, s, -$\dot{C}$(CH_3)$_2$), 1.72 (3H, s, -OCOCH_3), 2.95 (1H, m, -$C\underline{H}$(CH_3)$_2$), 4.05 and 4.43 (ABq, each 1H and d, $J=11$ Hz, -$C\underline{H}_2$OCOCH_3), 6.45 (1H, s, C_6-H), 7.28 (2H, bs, C_{11}-H and C_{12}-H), 7.79 (1H, bs, C_{14}-H). Found: C, 77.46; H, 8.34%. Calcd for $C_{22}H_{28}O_3$: C, 77.61; H, 8.29%.

Catalytic Hydrogenation of 24. A mixture of **24** (280 mg), 10% Pd-C (200 mg), and 60% perchloric acid (0.2 ml) in ethyl acetate (7.0 ml) was stirred at room temperature for 7.5 h in an atmosphere of hydrogen. The mixture was filtered and the filtrate was washed with brine. The dried solution was evaporated *in vacuo* to give an oil (267 mg: 98.9%), whose IR and ^1H NMR spectra were identical with those of the authentic **11**.

6,20-Diacetoxyabieta-5,8,11,13-tetraen-7-one (25). A mixture of **22** (220.0 mg) and anhydrous sodium acetate (900 mg) in acetic anhydride (9.0 ml) was refluxed for 28.5 h. The reaction mixture was cooled and diluted with ether. The ether solution was washed with water and evaporated *in vacuo*. The residue was extracted with ether. The ether extract was washed successively with aqueous sodium hydrogencarbonate and brine, dried over sodium sulfate, and evaporated *in vacuo*. The crude product was purified by column chromatography on silica gel (20 g), using ether-benzene (3:97) as the eluent, to give **25** (191.6 mg: 77.9%), $[\alpha]_D$ +13.1° (*c* 2.68); IR: 1760, 1740, 1664, 1614 cm^{-1}; ^1H NMR: 1.28 (6H, d, $J=7$ Hz, -CH($C\underline{H}_3$)$_2$), 1.29 and 1.34 (each 3H and s, -$\dot{C}$(CH_3)$_2$), 1.77 (3H, s, C_{20}-OCOCH_3), 2.30 (3H, s, C_6-OCOCH_3), 2.94 (1H, m, -$C\underline{H}$(CH_3)$_2$), 3.88 and 4.56 (ABq, each 1H and d, $J=11$ Hz, -$C\underline{H}_2$OCOCH_3), 7.33 (2H, bs, C_{11}-H and C_{12}-H), 7.80 (1H, bs, C_{14}-H); MS (*m/e*): 398 (M^+).

Catalytic Hydrogenation of 25. A mixture of **25** (175.0 mg), 10% Pd-C (175 mg), and 60% perchloric acid (0.2 ml) was submitted to catalytic hydrogenation at room temperature for 9 h. After the same work-up as described for the preparation of **11**, the crude product was chromatographed on silica gel (15 g), using benzene as the eluent, to give **11** (41.6 mg: 28.8%). Further elution with ether-benzene (1:99) afforded, without further separation, a mixture (90.3 mg: 53.2%) of 6α,20-diacetoxyabieta-8,11,13-triene (**26**) and 6β,20-diacetoxyabieta-8,11,13-triene (**27**) in a ratio of *ca.* 1:1. ^1H NMR of **26** ($CDCl_3$): 0.87 and 1.04 (each 3H and s, -$\dot{C}$(CH_3)$_2$), 1.69 and 1.98 (each 3H and s, C_6-OCOCH_3 and C_{20}-OCOCH_3), 4.32 (2H, s, -$C\underline{H}_2$OCOCH_3), 5.44 (1H, m, $W_{1/2}=14$ Hz, $C_{6\beta}$-H). ^1H NMR of **27** ($CDCl_3$): 1.04 and 1.07 (each 3H and s, -$\dot{C}$(CH_3)$_2$), 1.99 and 2.02 (each 3H and s, C_6-OCOCH_3 and C_{20}-OCOCH_3), 4.45 and 4.80 (ABq, each 1H and d, $J=12$ Hz, -$C\underline{H}_2$OCOCH_3), 5.65 (1H, m, $W_{1/2}=10$ Hz, $C_{6\alpha}$-H).

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7) Yields are based on the starting material consumed.

8) A personal communication from Dr. Yatagai informed us that the melting point of natural piciferol was raisen to 146.6—148.2 °C by recrystallization and no depression resulted when it was mixed with the synthetic pisiferol (**1**).