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The Synthesis of Methyl (15*S*)-16-Hydroxydehydroabietate and Its (15*R*)-Epimer

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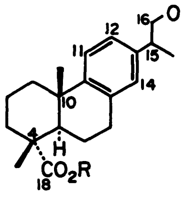
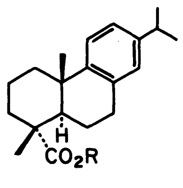
In order to elucidate the absolute configuration of C-15 in natural 16-hydroxydehydroabietic acid, a metabolite of (+)-dehydroabietic acid in rabbits, methyl (+)-dehydroabietate was transformed into methyl (15*S*)-16-hydroxy-8,11,13-abietatrien-18-oate (**3a**) and its (15*R*)-epimer (**3b**). The synthetic **3a** was identical with a methyl ester derived from the natural acid. Thus, the absolute configuration of C-15 in natural 16-hydroxydehydroabietic acid was conclusively assigned as an *S*-configuration.

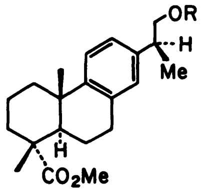
16-Hydroxydehydroabietic acid (**1**), a biotransformation product of (+)-dehydroabietic acid (**2**), has been isolated independently as its methyl ester (**3**) by three groups, Ekman and Sjöholm,1) Asakawa et al.,2) and Nakashima et al.3) However the absolute configuraion of C-15 in the biotransformation product has remained unsettled. In order to elucidate the unknown stereochemistry at C-15, we have now attempted the syntheses of methyl (15*S*)-16-hydroxy-8,11,13-abietatrien-18-oate (**3a**) and its (15*R*)-epimer (**3b**) starting from methyl (+)-dehydroabietate (**4**).

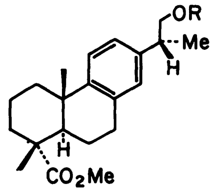


1 R=H
3 R=Me



2 R=H
4 R=Me





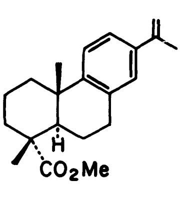
3a R=H 3b
20a $R=COC_6H_4NO_2(p)$ 20b

Dehydrogenation of **4** with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone in refluxing 1,4-dioxane afforded the corresponding isopropenyl compound (**5**) which was immediately submitted to hydroboration-oxidation to give a mixture of the desired C-15 epimeric methyl 16-hydroxy-8,11,13-abietatrien-18-oates (**3**) in 39% yield from **4**. Compound **3** was then transformed into a mixture of the corresponding benzoates (**6**) by heating with benzoyl chloride in pyridine in a quantitative yield. Since a separation of the C-15 epimers in the mixture of **3** or **6** was unsuccessful, the benzoate **6** was converted into a C-15 epimeric mixture (ca. 1:1 ratio) of 12-acetyl compounds **7a,b** by Friedel-Crafts acylation using acetyl chloride and anhydrous aluminum chloride in dichloromethane in 86% yield. This mixture of **7a,b** was carefully separated by repeated column chromatography on silica gel and recrystallization to afford a pure crystalline methyl 12-acetyl-16-benzoyloxy-8,11,13-abietatrien-18-oate (**7a**), mp 113—114 °C, and its C-15 epimer (**7b**), mp 140—141.5 °C. The absolute configuration of C-15 in these diastereomers **7a** and **7b** were determined by the following chemical correlation. The Baeyer-Villiger oxidation of **7a** and **7b** with *m*-chloroperbenzoic acid and *p*-toluenesulfonic acid in refluxing 1,2-dichloroethane, followed by hydrolysis of the resulting acetates, **8a** (91%) and **8b** (85%), with aqueous sodium hydroxide in refluxing methanol, afforded the C-15 epimeric methyl 12,16-dihydroxy-8,11,13-abietatrien-18-oates **9a** (98%) and **9b** (92%), respectively. For the protection of the hydroxyl groups, the 12,16-diol **9a** was treated with a mixture of chloromethyl methyl ether, potassium iodide, and anhydrous potassium carbonate in refluxing ethyl methyl ketone to give a 12,16-methylenedioxy compound **10a** (55%) together with a 12,16-bis(methoxymethyl) ether **11a** (4%) and a 16-methoxymethyl ether **12a** (18%). The hydrolysis of **12a** with dilute hydrochloric acid in refluxing tetrahydrofuran produced **9a** and **10a** in 62 and 27% yields, respectively. A reduction of **10a** with lithium aluminum hydride in ether followed by tosylation of the resulting alcohol with *p*-toluenesulfonyl chloride in pyridine afforded the tosylate **13a** (95%). This was further treated with sodium iodide and zinc powder in *N*,*N*-dimethylformamide at 120—125 °C to give a 4,4-dimethyl compound **14a** (64%). The hydrolysis of **14a** with dilute hydrochloric acid in refluxing ethanol produced the known (15*S*)-16-hydroxyferruginol(**15a**)4,5) in 78% yield. Thus, the absolute configurations of C-15 in **7a** and its derivatives **8a**—**14a** were assigned as the same *S*-configuration.

Similarly, the 12,16-diol **9b** was also converted into the known (15*R*)-16-hydroxyferruginol (**15b**).4,5) Thus, the absolute configurations of C-15 in **7b** and its derivatives **8b**—**14b** were also assigned as the same *R*-configuration.

Subsequently, syntheses of methyl (15*S*)-16-hydroxy-8,11,13-abietatrien-18-oate (**3a**) and its (15*R*)-epimer (**3b**) were carried out as follows. Partial hydrolysis of methyl (15*S*)-12-acetoxy-16-benzoyloxy-8,11,13-abietatrien-18-oate (**8a**) with dilute hydrochloric acid in refluxing methanol afforded methyl (15*S*)-16-benzoyloxy-12-hydroxy-8,11,13-abietatrien-18-oate (**16a**) in 87% yield. In order to remove the C-12 hydroxyl group, the phenolic compound **16a** was converted into the corresponding 1-phenyl-5-tetrazolyl ether **17a** (91%) by refluxing with 5-chloro-1-phenyl-1*H*-tetrazole and anhydrous potassium carbonate in ethyl methyl ketone. However, an attempt to hydrogenolyze this ether **17a** over 10% Pd–C in ethanol at room temperature gave no deoxygenation product and only the starting **17a** was recovered. Therefore, the 12,16-diol **9a** was treated with 5-chloro-1-phenyl-1*H*-tetrazole under the same conditions to produce methyl (15*S*)-16-hydroxy-12-(1-phenyl-1*H*-tetrazol-5-yloxy)-8,11,13-abietatrien-18-oate (**18a**: 48%) together with a dihydrobenzofuran derivative **19a** (37%) which was identical with authentic methyl (15*S*)-12,16-epoxy-8,11,13-abietatrien-18-oate.[6] Catalytic hydrogenolysis of **18a** over 10% Pd–C in ethanol at room temperature under an atmosphere of hydrogen afforded the desired methyl (15*S*)-16-hydroxy-8,11,13-abietatrien-18-oate (**3a**: 39%[7]), which gave a 4-nitrobenzoate (**20a**), mp 116—117 °C.

Similarly, methyl (15*R*)-12-acetoxy-16-benzoyloxy-8,11,13-abietatrien-18-oate (**8b**) was also transformed into methyl (15*R*)-16-hydroxy-8,11,13-abietatrien-18-oate (**3b**), which gave a 4-nitrobenzoate (**20b**), mp 133—134 °C. The methyl ester of the metabolite of (+)-dehydroabietic acid (**2**) in rabbits[2] and its 4-nitrobenzoate (mp 116—117 °C) were identical with the synthetic **3a** and **20a**, respectively.



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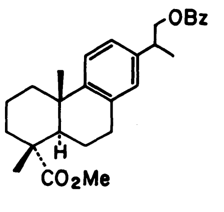

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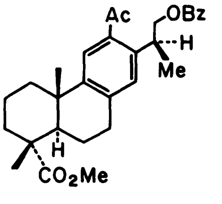
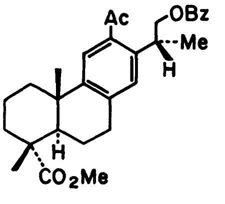
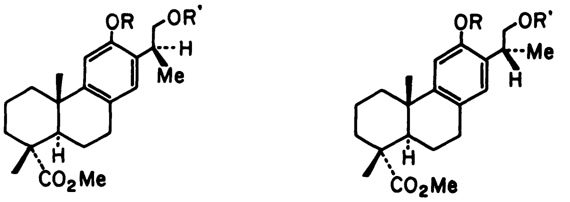


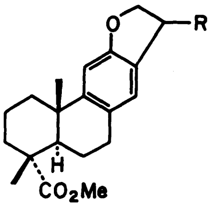
7a



7b

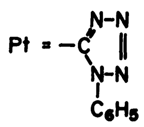


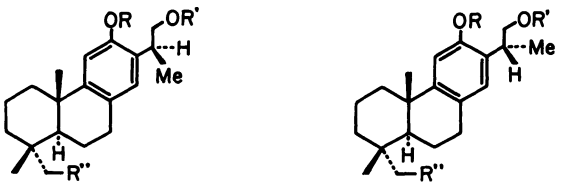
8a	R=Ac, R'=Bz	8b
9a	R=R'=H	9b
10a	R·R'=–CH$_2$–	10b
11a	R=R'=CH$_2$OMe	11b
12a	R=H, R'=CH$_2$OMe	12b
16a	R=H, R'=Bz	16b
17a	R=Pt, R'=Bz	17b
18a	R=Pt, R'=H	18b



19a R=β-Me
19b R=α-Me

Bz = COC$_6$H$_5$





13a	R·R'=–CH$_2$–, R''=OTs	13b
14a	R·R'=–CH$_2$–, R''=H	14b
15a	R=R'=R''=H	15b

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; s: singlet, bs: broad singlet, d: doublet, bd: broad doublet, dd: double doublet, m: multiplet. The column chromatography was performed using Merck silica gel (0.063 mm).

Methyl 8,11,13,15-Abietatetraen-18-oate (5). A mixture of methyl (+)-dehydroabietate (**4**) (21.07 g) and 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (96%: 19.01 g) in 1,4-dioxane (210 ml) was refluxed for 4 h. The mixture was passed through an alumina (Merck Act. II—III, 200 g) column and the column was washed with benzene (600 ml). The eluate was evaporated in vacuo to give a crude **5** (16.88 g) as an oil, which was used, without purification, in the next reaction. IR 1715 and 1625 cm^{-1}, ^{1}H NMR δ=1.19 (3H, s, C$_{10}$–CH$_3$), 1.22 (3H, s, C$_4$–CH$_3$), 2.08 (3H, bs, C$_{15}$–CH$_3$), 3.61 (3H, s,

-CO$_2$CH$_3$), 4.88 (lH, bs) and 5.17 (1H, bs) (-C(CH$_3$)=C$\underline{\mathrm{H}}_2$), 6.93 (lH, s) and 7.05 (2H, s) (aromatic protons).

Methyl 16-Hydroxy-8,11,13-abietatrien-18-oate (3). A solution of borane-tetrahydrofuran complex (1 mol dm^{-3}: 27.0 ml) was added to a stirred solution of the crude **5** (16.88 g) in dry tetrahydrofuran (170 ml) at −15—−10 °C for 20 min under a stream of nitrogen. After the mixture had been stirred at −10—0 °C for 10 min and at 0—5 °C for 3 h, there were added successively aqueous tetrahydrofuran (50%: 11.8 ml), aqueous sodium hydroxide (12%: 11.8 ml), and hydrogen peroxide (30%: 11.8 ml) at −15—−5 °C. The mixture was stirred at −5—0 °C for 30 min and then at room temperature for 1 h, diluted with brine, 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 (0.063—0.200 mm, 200 g), using ether-benzene (3:97) as an eluent, to give mainly methyl dehydroabietate (**4**) (6.97 g). Further elution with ether-benzene (3:97 and then 6:94) afforded a mixture of C-15 epimers **3** (8.64 g: 39.0% from **4**) as an oil which, after standing at room temperature, was solidified. IR 3580, 3450, and 1720 cm^{-1}; ^{1}H NMR (90 MHz, CDCl$_3$) δ=1.19 (3H, s, C$_{10}$-CH$_3$), 1.23 (3H, d, J=7 Hz, C$_{15}$-CH$_3$), 1.27 (3H, s, C$_4$-CH$_3$), 3.67 (2H, d, J=7 Hz, -C$\underline{\mathrm{H}}_2$OH), 3.67 (3H, s, -CO$_2$CH$_3$), 6.86 (1H, bs, C$_{14}$-H), 6.96 (1H, dd, J=9 and 2 Hz, C$_{12}$-H), 7.18 (1H, d, J=9 Hz, C$_{11}$-H). Found: C, 76.14; H, 9.38%. Calcd for C$_{21}$H$_{30}$O$_3$: C, 76.32; H, 9.15%.

Methyl 16-Benzoyloxy-8,11,13-abietatrien-18-oate (6). A mixture of **3** (7.992 g) and benzoyl chloride (4.18 ml) in pyridine (15.0 ml) was heated at 75—80 °C for 1.5 h. The mixture was cooled, poured into ice-dilute hydrochloric acid, and extracted with ether. The ether extract was washed successively with dilute hydrochloric acid, aqueous sodium hydrogencarbonate, and brine. The dried solution was evaporated in vacuo. The residue was chromatographed on silica gel (0.063—0.200 mm, 200 g), using hexane-benzene (2:8) as an eluent, to give an oily mixture of C-15 epimeric benzoates **6** (10.337 g: 98.4%). IR 1720 cm^{-1}, ^{1}H NMR (90 MHz, CDCl$_3$) δ=1.19 (3H, s, C$_{10}$-CH$_3$), 1.26 (3H, s, C$_4$-CH$_3$), 1.36 (3H, d, J=7 Hz, C$_{15}$-CH$_3$), 3.14 (1H, m, C$_{15}$-H), 3.65 (3H, s, -CO$_2$CH$_3$), 4.27 (1H, dd, J=11 and 7 Hz) and 4.41 (1H, dd, J=11 and 7 Hz) (C$_{15}$-CH$_2$O-), 6.92 (1H, bs, C$_{14}$-H), 7.00 (1H, dd, J=9 and 2 Hz, C$_{12}$-H), 7.18 (1H, d, J=9 Hz, C$_{11}$-H), 7.25—7.6 (3H, m) and 7.98 (2H, dd, J=8 and 2 Hz) (-OCOC$_6$H$_5$). Found: C, 77.54; H, 8.19%. Calcd for C$_{28}$H$_{34}$O$_4$: C, 77.39; H, 7.89%.

Methyl (15*S*)-12-Acetyl-16-benzoyloxy-8,11,13-abietatrien-18-oate (7a) and Its (15*R*)-Epimer (7b). Anhydrous aluminum chloride (1.70 g) was added at −10 °C to a stirred solution of **6** (1.387 g) and acetyl chloride (0.91 ml) in dichloromethane (15 ml). The mixture was stirred at this temperature for 15 min and then at room temperature for 64 h, poured into ice-dilute hydrochloric acid, and extracted with ether. The ether extract was washed successively with aqueous sodium hydrogencarbonate and brine, dried, and evaporated in vacuo. The residue was chromatographed on silica gel (50 g), using hexane-chloroform (2:8) as an eluent, to give a C-15 epimeric mixture (ca. 1:1 ratio) of methyl 12-acetyl-16-benzoyloxy-8,11,13-abietatrien-18-oate (**7a,b**) (1.314 g: 86.4%). The mixture (**7a,b**) was separated into the pure **7a**, mp 113—114 °C (from methanol), [α]$_D$ +49.2° (*c* 2.32), IR 1718 and 1680 cm^{-1}, and **7b**, mp 140—141.5 °C (from methanol), [α]$_D$ +49.1° (*c* 3.95), IR 1718 and 1680 cm^{-1}, by repeated column chromatography on silica gel and recrystallization. ^{1}H NMR of **7a** (90 MHz) δ=1.19 (3H, s, C$_{10}$-CH$_3$), 1.22 (3H, s, C$_4$-CH$_3$), 1.31 (3H, d, J=7 Hz, C$_{15}$-CH$_3$), 2.47 (3H, s, C$_{12}$-COCH$_3$), 3.62 (3H, s, -CO$_2$CH$_3$), 3.87 (1H, m, C$_{15}$-H), 4.33 (2H,d, J=7 Hz, C$_{15}$-CH$_2$O-), 7.03 (1H, s, C$_{14}$-H), 7.39 (1H, s, C$_{11}$-H), 7.2—7.45 (3H, m) and 7.92 (2H, dd, J=8 and 2 Hz) (-OCOC$_6$H$_5$). Anal. of **7a**; Found: C, 75.72; H, 7.89%. Calcd for C$_{30}$H$_{36}$O$_5$: C, 75.60; H, 7.61%. ^{1}H NMR of **7b** (90 MHz) δ=1.19 (3H, s, C$_{10}$-CH$_3$), 1.22 (3H, s, C$_4$-CH$_3$), 1.32 (3H, d, J=7 Hz, C$_{15}$-CH$_3$), 2.47 (3H, s, C$_{12}$-COCH$_3$), 3.62 (3H, s, -CO$_2$CH$_3$), 3.88 (1H, m, C$_{15}$-H), 4.30 (2H, d, J=7 Hz, C$_{15}$-CH$_2$O-), 7.02 (1H, s, C$_{14}$-H), 7.39 (1H, s, C$_{11}$-H), 7.2—7.45 (3H, m) and 7.92 (2H, dd, J=8 and 2 Hz) (-OCOC$_6$H$_5$). Anal. of **7b**; Found: C, 75.42; H, 7.91%. Calcd for C$_{30}$H$_{36}$O$_5$: C, 75.60; H, 7.61%.

Methyl (15*S*)-12-Acetoxy-16-benzoyloxy-8,11,13-abietatrien-18-oate (8a) and Its (15*R*)-Epimer (8b). a): A mixture of **7a** (1.655 g), *m*-chloroperbenzoic acid (80%: 1.498 g), and *p*-toluenesulfonic acid (30 mg) in 1,2-dichloroethane (15 ml) was refluxed for 3 h. The mixture was cooled, diluted with ether, and the ether solution was washed successively with aqueous potassium iodide, aqueous sodium thiosulfate, aqueous sodium hydrogencarbonate, and brine. The dried solution was evaporated in vacuo. The residue was chromatographed on silica gel (18 g), using ether-benzene (3:97) as an eluent, to give **8a** (1.552 g: 90.8%) which was recrystallized from methanol, mp 126—128 °C, [α]$_D$ +33.5° (*c* 3.17), IR 1755 and 1718 cm^{-1}, ^{1}H NMR δ=1.23 (6H, s, C$_4$-CH$_3$ and C$_{10}$-CH$_3$), 1.28 (3H, d, J=7 Hz, C$_{15}$-CH$_3$), 2.25 (3H, s, C$_{12}$-OCOCH$_3$), 3.25 (1H, m, C$_{15}$-H), 3.62 (3H, s, -CO$_2$CH$_3$), 3.75—4.5 (2H, m, C$_{15}$-CH$_2$O-), 6.77 (1H, s) and 6.90 (1H, s) (C$_{11}$-H and C$_{14}$-H), 7.27—7.54 (3H, m) and 7.95 (2H, dd, J=8 and 2 Hz) (-OCOC$_6$H$_5$). Found: C, 72.83; H, 7.50%. Calcd for C$_{30}$H$_{36}$O$_6$: C, 73.14; H, 7.37%.

b): A mixture of **7b** (1.804 g), *m*-chloroperbenzoic acid (80%: 1.470 g), and *p*-toluenesulfonic acid (30 mg) in 1,2-dichloroethane (20 ml) was refluxed for 3.5 h. After the work-up (as described in **a)**) the crude product was purified by column chromatography on silica gel (40 g), using ether-benzene (3:97) as an eluent, to give the recovered **7b** (152 mg) and an oily **8b** (1.585 g: 85.1%) [α]$_D$ +66.8° (*c* 5.79), IR 1753 and 1718 cm^{-1}, ^{1}H NMR δ=1.20 (3H, s) and 1.24 (3H, s) (C$_4$-CH$_3$ and C$_{10}$-CH$_3$), 1.29 (3H, d, J=7 Hz, C$_{15}$-CH$_3$), 2.25 (3H, s, C$_{12}$-OCOCH$_3$), 3.27 (1H, m, C$_{15}$-H), 3.60 (3H, s, -CO$_2$CH$_3$), 3.9—4.5 (2H, m, C$_{15}$-CH$_2$O-), 6.78 (1H, s) and 6.90 (1H, s) (C$_{11}$-H and C$_{14}$-H), 7.25—7.6 (3H, m) and 7.97 (2H, dd, J=8 and 2 Hz) (-OCOC$_6$H$_5$). Found: C, 73.35; H, 7.45%. Calcd for C$_{30}$H$_{36}$O$_6$: C, 73.14; H, 7.37%.

Methyl (15*S*)-12,16-Dihydroxy-8,11,13-abietatrien-18-oate (9a) and Its (15*R*)-Epimer (9b). a): A mixture of **8a** (544 mg) and aqueous sodium hydroxide (20%: 1.5 ml) in methanol (6.0 ml) was refluxed for 1 h. The mixture was cooled, acidified with dilute hydrochloric acid, and extracted with ether. The ether extract was washed successively with aqueous sodium hydrogencarbonate and brine, dried, and evaporated in vacuo. The residue was chromatographed on silica gel (10 g), using ether-benzene (1:9) as an eluent, to give **9a** (375 mg: 98.0%) which was recrystallized from ether-hexane, mp 105—107 °C, [α]$_D$ +50.0° (*c* 3.20), IR 3600, 3325, and 1720 cm^{-1}; ^{1}H NMR (90 MHz) δ=1.13 (3H, s, C$_{10}$-CH$_3$), 1.19 (3H, d, J=7 Hz,

C_{15}–CH_3), 1.20 (3H, s, C_4–CH_3), 3.02 (1H, m, C_{15}–H), ca. 3.6 (2H, m, overlap, C_{15}–$C\underline{H}_2OH$), 3.61 (3H, s, –CO_2CH_3), 6.57 (2H, s, C_{11}–H and C_{14}–H). Found: C, 72.63; H, 8.86%. Calcd for $C_{21}H_{30}O_4$: C, 72.80; H, 8.73%.

b): A mixture of **8b** (1.207 g) and aqueous sodium hydroxide (20%: 3.0 ml) in methanol (10 ml) was refluxed for 1 h. After the work-up (as described in **a)**) the crude product was purified by column chromatography on silica gel (16 g), using ether–benzene (1:9) as an eluent, to give an oily **9b** (662 mg: 91.9%), $[\alpha]_D$ +65.5° (*c* 8.11), IR 3600, 3325, and 1720 cm^{-1}; ^1H NMR (90 MHz) δ=1.11 (3H, s, C_{10}–CH_3), 1.17 (3H, d, *J*=7 Hz, C_{15}–CH_3), 1.19 (3H, s, C_4–CH_3), 3.02 (1H, m, C_{15}–H), ca. 3.6 (2H, m, overlap, C_{15}–$C\underline{H}_2OH$), 3.60 (3H, s, –CO_2CH_3), 6.57 (2H, s, C_{11}–H and C_{14}–H). Found: C, 72.78; H, 8.85%. Calcd for $C_{21}H_{30}O_4$: C, 72.80; H, 8.73%.

Reactions of 9a and 9b with Chloromethyl Methyl Ether. a): A stirred mixture of **9a** (584.0 mg), chloromethyl methyl ether (0.89 ml), potassium iodide (2.34 g), and anhydrous potassium carbonate (2.34 g) in ethyl methyl ketone (10 ml) was refluxed for 5 h. The mixture was cooled, diluted with water, and extracted with ether. The ether extract was washed successively with aqueous sodium thiosulfate and brine, dried, and evaporated in vacuo. The residue was chromatographed on silica gel (20 g), using ether–benzene (1:99) as an eluent, to give methyl (15*S*)-12,16-methylenedioxy-8,11,13-abietatrien-18-oate (**10a**) (332.0 mg: 54.8%) which was recrystallized from methanol, mp 154—155 °C, $[\alpha]_D$ +27.2° (*c* 1.62), IR 1715 cm^{-1}, ^1H NMR (90 MHz) δ=1.19 (3H, s) and 1.21 (3H, s) (C_4–CH_3 and C_{10}–CH_3), 1.28 (3H, d, *J*=7 Hz, C_{15}–CH_3), 2.6—3.0 (3H, m, C_7–H_2 and C_{15}–H), 3.53 (1H, dd, *J*=12 and 2 Hz) and 3.82 (1H, dd, *J*=12 and 4 Hz) (C_{15}–CH_2O–), 3.61 (3H, s, –CO_2CH_3), 4.52 (1H, d, *J*=7 Hz) and 5.16 (1H, d, *J*=7 Hz) (–OCH_2O–), 6.65 (1H, s, C_{14}–H), 6.72 (1H, s, C_{11}–H). Found: C, 73.59; H, 8.63%. Calcd for $C_{22}H_{30}O_4$: C, 73.71; H, 8.44%.

Subsequent elution with ether–benzene (2:98) gave methyl (15*S*)-12,16-bis(methoxymethoxy)-8,11,13-abietatrien-18-oate (**11a**) as an oil (29.0 mg: 4.0%), $[\alpha]_D$ +52.7° (*c* 0.74), IR 1720 cm^{-1}, ^1H NMR δ=1.19, (3H, s, C_{10}–CH_3), 1.20 (3H, d, *J*=7 Hz, C_{15}–CH_3), 1.23 (3H, s, C_4–CH_3), 3.20 (3H, s, C_{16}–$OCH_2OC\underline{H}_3$), 3.42 (3H, s, C_{12}–$OCH_2OC\underline{H}_3$), 3.60 (3H, s, –CO_2CH_3), 4.46 (2H, s, C_{16}–$OC\underline{H}_2OCH_3$), 5.03 (2H, s, C_{12}–$OC\underline{H}_2OCH_3$), 6.67 (1H, s) and 6.78 (1H, s) (C_{11}–H and C_{14}–H). Found: C, 69.28; H, 9.06%. Calcd for $C_{25}H_{38}O_6$: C, 69.09; H, 8.81%.

Further elution with ether–benzene (5:95) afforded methyl (15*S*)-12-hydroxy-16-methoxymethoxy-8,11,13-abietatrien-18-oate (**12a**) (119.5 mg: 18.2%) which was recrystallized from acetone–hexane, mp 81.5—82.5 °C, $[\alpha]_D$ +50.3° (*c* 1.53), IR 3325 and 1720 cm^{-1}, ^1H NMR δ=1.17 (3H, s, C_{10}–CH_3), 1.22 (3H, s, C_4–CH_3), 1.26 (3H, d, *J*=7 Hz, C_{15}–CH_3), 3.23 (3H, s, C_{16}–$OCH_2OC\underline{H}_3$), 3.60 (3H, s, –CO_2CH_3), 4.54 (2H, s, C_{16}–$OC\underline{H}_2OCH_3$), 6.57 (2H, bs, C_{11}–H and C_{14}–H), 6.69 (1H, s, C_{12}–OH). Found: C, 70.98; H, 8.97%. Calcd for $C_{23}H_{34}O_5$: C, 70.74; H, 8.78%.

b): A stirred mixture of **9b** (572.0 mg), chloromethyl methyl ether (0.87 ml), potassium iodide (2.28 g), and anhydrous potassium carbonate (2.28 g) in ethyl methyl ketone (10 ml) was refluxed for 5 h. After the work-up (as described in **a)**) the crude product was purified by column chromatography on silica gel (16 g), using ether–benzene (2:98) as an eluent, to give methyl (15*R*)-12,16-methylenedioxy-8,11,13-abietatrien-18-oate (**10b**) (213.0 mg: 36.0%) which was recrystallized from methanol, mp 134—135 °C, $[\alpha]_D$ +93.3° (*c* 2.53), IR 1718 cm^{-1}, ^1H NMR (90 MHz) δ=1.16 (3H, s, C_{10}–CH_3), 1.20 (3H, s, C_4–CH_3), 1.24 (3H, d, *J*=7 Hz, C_{15}–CH_3), 2.65—3.0 (3H, m, C_7–H_2 and C_{15}–H), 3.56 (1H, dd, *J*=12 and 2 Hz) and 3.78 (1H, dd, *J*=12 and 4 Hz) (C_{15}–CH_2O–), 3.61 (3H, s, –CO_2CH_3), 4.57 (1H, d, *J*=7 Hz) and 5.12 (1H, d, *J*=7 Hz) (–OCH_2O–), 6.63 (1H, s, C_{14}–H), 6.71 (1H, s, C_{11}–H). Found: C, 73.62; H, 8.74%. Calcd for $C_{22}H_{30}O_4$: C, 73.71; H, 8.44%.

Subsequent elution gave methyl (15*R*)-12,16-bis(methoxymethoxy)-8,11,13-abietatrien-18-oate (**11b**) as an oil (72.2 mg: 10.1%), $[\alpha]_D$ +54.2° (*c* 2.59), IR 1720 cm^{-1}, ^1H NMR δ=1.18 (3H, s, C_{10}–CH_3), 1.18 (3H, d, *J*=7 Hz, C_{15}–CH_3), 1.21 (3H, s, C_4–CH_3), 3.21 (3H,s, C_{16}–$OCH_2OC\underline{H}_3$), 3.42 (3H, s, C_{12}–$OCH_2OC\underline{H}_3$), 3.59 (3H, s, –CO_2CH_3), 4.43 (2H, s, C_{16}–$OC\underline{H}_2OCH_3$), 5.03 (2H, s, C_{12}–$OC\underline{H}_2OCH_3$), 6.67 (1H, s) and 6.79 (1H, s) (C_{11}–H and C_{14}–H). Found: C, 68.89; H, 8.95%. Calcd for $C_{25}H_{38}O_6$: C, 69.09; H, 8.81%.

Further elution with ether–benzene (5:95) afforded methyl (15*R*)-12-hydroxy-16-methoxymethoxy-8,11,13-abietatrien-18-oate (**12b**) (162.9 mg: 25.3%) which was recrystallized from acetone–hexane, mp 118—119 °C, $[\alpha]_D$ +61.2° (*c* 2.06), IR 3330 and 1720 cm^{-1}, ^1H NMR δ=1.15 (3H, s, C_{10}–CH_3), 1.22 (3H, s, C_4–CH_3), 1.26 (3H, d, *J*=7 Hz, C_{15}–CH_3), 3.26 (3H, s, C_{16}–$OCH_2OC\underline{H}_3$), 3.60 (3H, s, –CO_2CH_3), 4.54 (2H, s, C_{16}–$OC\underline{H}_2OCH_3$), 6.57 (2H, bs, C_{11}–H and C_{14}–H), 6.77 (1H, s, C_{12}–OH). Found: C, 70.79; H, 9.04%. Calcd for $C_{23}H_{34}O_5$: C, 70.74; H, 8.78%.

Hydrolyses of 11b, 12a, and 12b. a): A mixture of **11b** (20.0 mg) and dilute hydrochloric acid (15%: 0.15 ml) in tetrahydrofuran (1.5 ml) was refluxed for 2.5 h. The mixture was cooled, diluted with ether, and the ether solution was washed with brine. The dried solution was evaporated in vacuo. The residue was chromatographed on silica gel (6 g), using ether–benzene (1:9) as an eluent, to give a 12,16-diol (12.8 mg: 80.3%), the IR and ^1H NMR spectra of which were identical with those of the authentic **9b**.

b): A mixture of **12a** (68.0 mg) and dilute hydrochloric acid (15%: 0.3 ml) in tetrahydrofuran (3.0 ml) was refluxed for 2.5 h. After the work-up (as described in **a)**) the crude product was chromatographed on silica gel (10 g), using ether–benzene (3:97) as an eluent, to give a 12,16-methylenedioxy compound (16.6 mg: 26.6%), the IR and ^1H NMR spectra of which were identical with those of the authentic **10a**. Further elution with ether–benzene (1:9) afforded a 12,16-diol (37.4 mg: 62.0%), the IR and ^1H NMR spectra of which were identical with those of the authentic **9a**.

c): A mixture of **12b** (111.0 mg) and dilute hydrochloric acid (15%: 0.4 ml) in tetrahydrofuran (4.0 ml) was refluxed for 2.5 h. After the work-up (as described in **a)**) the crude product was chromatographed on silica gel (8 g), using ether–benzene (3:97) as an eluent, to give a 12,16-methylenedioxy compound (22.9 mg: 22.5%), the IR and ^1H NMR spectra of which were identical with those of the authentic **10b**. Further elution with ether–benzene (1:9) afforded a 12,16-diol (67.4 mg: 68.4%), the IR and ^1H NMR spectra of which were identical with those of the authentic **9b**.

(15*S*)-12,16-Methylenedioxy-18-tosyloxy-8,11,13-abietatriene (13a) and Its (15*R*)-Epimer (13b). a): A mixture of

10a (146 mg) and lithium aluminum hydride (20 mg) in dry ether (4.0 ml) was stirred at room temperature for 1 h. The mixture was poured into ice-dilute hydrochloric acid and extracted with ether. The ether extract was washed with brine, dried, and evaporated in vacuo to give a crude alcohol (134 mg) as an oil, IR 3630 and 3475 cm^{-1}.

A mixture of the above crude alcohol (134 mg) and *p*-toluenesulfonyl chloride (93 mg) in pyridine (1.5 ml) was heated at 80—85 °C for 4 h. The mixture was cooled, poured into ice-dilute hydrochloric acid, and extracted with ether. The ether extract was washed successively with aqueous sodium hydrogencarbonate and brine, dried, and evaporated in vacuo. The residue was chromatographed on silica gel (8 g), using ether–benzene (2:98) as an eluent, to give **13a** (188 mg: 95.3%) which was recrystallized from methanol, mp 113—114 °C, $[\alpha]_D$ +16.1 ° (*c* 2.36), IR 1360 and 1178 cm^{-1}, ^{1}H NMR δ=0.88 (3H, s, C_4–CH_3), 1.17 (3H, s, C_{10}–CH_3), 1.28 (3H, d, *J*=7 Hz, C_{15}–CH_3), 2.44 (3H, s, $-C_6H_4C\underline{H}_3$), 3.3—4.0 (4H, m, C_4–$C\underline{H}_2OTs$ and C_{15}–CH_2O–), 4.51 (1H, d, *J*=7 Hz) and 5.15 (1H, d, *J*=7 Hz) (–OCH_2O–), 6.66 (1H, s, C_{14}–H), 6.72 (1H, s, C_{11}–H), 7.28 (2H, d, *J*=9 Hz) and 7.74 (2H, d, *J*=9 Hz) ($-C_6\underline{H}_4CH_3$). Found: C, 69.60; H, 7.75%. Calcd for $C_{28}H_{36}O_5S$: C, 69.40; H, 7.48%.

b): A mixture of **10b** (182 mg) and lithium aluminum hydride (25 mg) in dry ether (5.0 ml) was stirred at room temperature for 1 h to give a crude alcohol (170 mg) as an oil, IR 3625 and 3460 cm^{-1}

The above crude alcohol (170 mg) was tosylated with *p*-toluenesulfonyl chloride (116 mg) in pyridine (2.0 ml) at 80—85 °C for 4 h. After the work-up (as described in **a)**) the crude product was purified by column chromatography on silica gel (8 g), using ether–benzene (1:99) as an eluent, to give **13b** (220 mg: 89.4%) which was recrystallized from methanol, mp 155—156 °C, $[\alpha]_D$ +70.7 ° (*c* 2.05), IR 1358 and 1174 cm^{-1}, ^{1}H NMR δ=0.87 (3H, s, C_4–CH_3), 1.13 (3H, s, C_{10}–CH_3), 1.24 (3H, d, *J*=7 Hz, C_{15}–CH_3), 2.43 (3H, s, $-C_6H_4C\underline{H}_3$), 3.3—4.0 (4H, m, C_4–$C\underline{H}_2OTs$ and C_{15}–CH_2O–), 4.51 (1H, d, *J*=7 Hz) and 5.08 (1H, d, *J*=7 Hz) (–OCH_2O–), 6.61 (1H, s, C_{14}–H), 6.69 (1H, s, C_{11}–H), 7.24 (2H, d, *J*=9 Hz) and 7.68 (2H, d, *J*=9 Hz) ($-C_6\underline{H}_4CH_3$). Found: C, 69.55; H, 7.68%. Calcd for $C_{28}H_{36}O_5S$: C, 69.40; H, 7.48%.

(15*S*)-12,16-Methylenedioxy-8,11,13-abietatriene (14a) and Its (15*R*)-Epimer (14b). a): A stirred mixture of **13a** (163.0 mg), sodium iodide (252 mg), and zinc powder (220 mg) in *N,N*-dimethylformamide (3.0 ml) was heated at 120—125 °C for 6 h. The mixture was cooled, diluted with ether, and then filtered. The filtrate was poured into dilute hydrochloric acid and extracted with ether. The ether extract was washed successively with aqueous sodium thiosulfate and brine, dried, and evaporated in vacuo. The residue was chromatographed on silica gel (7 g), using benzene as an eluent, to give an oily **14a** (68.0 mg: 64.4%), $[\alpha]_D$ +33.9 ° (*c* 3.30), ^{1}H NMR δ=0.94 (6H, s, $-\overset{|}{C}(CH_3)_2$), 1.16 (3H, s, C_{10}–CH_3), 1.28 (3H, d, *J*=7 Hz, C_{15}–CH_3), 3.35—3.95 (2H, m, C_{15}–CH_2O–), 4.50 (1H, d, *J*=7 Hz) and 5.13 (1H, d, *J*=7 Hz) (–OCH_2O–), 6.62 (1H, s, C_{14}–H), 6.71 (1H, s, C_{11}–H). Found: C, 80.48; H, 9.53%. Calcd for $C_{21}H_{30}O_2$: C, 80.21; H, 9.62%. Further elution with ether–benzene (6:94) afforded the recovered **13a** (24.9 mg: 15.3%).

b): A stirred mixture of **13b** (150.0 mg), sodium iodide (232 mg) , and zinc powder (202 mg) in *N,N*-dimethylformamide (4.0 ml) was heated at 120—125 °C for 6 h. After the work-up (as described in **a)**) the crude product was purified by column chromatography on silica gel (8 g), using benzene as an eluent, to give an oily **14b** (59.2 mg: 60.8%), $[\alpha]_D$ +101 ° (*c* 1.91), ^{1}H NMR δ=0.94 (6H, s, $-\overset{|}{C}(CH_3)_2$), 1.14 (3H, s, C_{10}–CH_3), 1.26 (3H, d, *J*=7 Hz, C_{15}–CH_3), 3.35—3.95 (2H, m, C_{15}–CH_2O–), 4.54 (1H, d, *J*=7 Hz) and 5.13 (1H,d, *J*=7 Hz) (–OCH_2O–), 6.63 (1H, s, C_{14}–H), 6.72 (1H, s, C_{11}–H). Found: C, 80.15; H, 9.55%. Calcd for $C_{21}H_{30}O_2$: C, 80.21; H, 9.62%.

Further elution with ether–benzene (6:94) afforded the recovered **13b** (32.1 mg: 21.4%) and (15*R*)-12,16-methylenedioxy-8,11,13-abietatrien-18-ol (9.9 mg: 9.7%).

(15*S*)-16-Hydroxyferruginol (15a) and Its (15*R*)-Epimer (15b). a): A mixture of **14a** (63.0 mg) and dilute hydrochloric acid (15%: 0.2 ml) in ethanol (2.0 ml) was refluxed for 6 h. The mixture was cooled and diluted with ether. The ether solution was washed with brine, dried, and evaporated in vacuo. The residue was chromatographed on silica gel (7 g), using ether–benzene (1:9) as an eluent, to give **15a** (47.4 mg: 78.4%) which was recrystallized from acetone–hexane, mp 177—178°C, $[\alpha]_D$ +45.5 ° (*c* 0.51), IR (KBr) 3555 and 3275 cm^{-1}, ^{1}H NMR (90 MHz, $CDCl_3$) δ=0.91 (6H, s, $-\overset{|}{C}(CH_3)_2$), 1.16 (3H, s, C_{10}–CH_3), 1.26 (3H, d, *J*=7 Hz, C_{15}–CH_3), 3.15 (1H, m, C_{15}–H), 3.64 (1H, dd, *J*=10 and 7 Hz) and 3.88 (1H, dd, *J*=10 and 4 Hz) (C_{15}–$C\underline{H}_2OH$), 6.74 (2H, s, C_{11}–H and C_{14}–H). Found: C, 79.31; H, 10.18%. Calcd for $C_{20}H_{30}O_2$: C, 79.42; H, 10.00%. The physical and spectral data of **15a** were identical with those of the authentic (15*S*)-16-hydroxyferruginol.[4,5)]

b): A mixture of **14b** (50.2 mg) and dilute hydrochloric acid (15%: 0.2 ml) in ethanol (2.0 ml) was refluxed for 5.5 h. After the work-up (as described in **a)**) the crude product was purified by column chromatography on silica gel (6 g), using ether–benzene (1:9) as an eluent, to give **15b** (38.1 mg: 78.9%) which was recrystallized from ether–hexane, mp 139—140 °C, $[\alpha]_D$ +65.7° (*c* 0.34), IR (KBr) 3520 and 3300 cm^{-1}, ^{1}H NMR (90 MHz, $CDCl_3$) δ=0.89 (3H, s) and 0.91 (3H, s) ($-\overset{|}{C}(CH_3)_2$), 1.13 (3H, s, C_{10}–CH_3), 1.24 (3H, d, *J*=7 Hz, C_{15}–CH_3), 3.15 (1H, m, C_{15}–H), 3.64 (1H, dd, *J*=10 and 7 Hz) and 3.88 (1H, dd, *J*=10 and 4 Hz) (C_{15}–$C\underline{H}_2OH$), 6.72 (2H, s, C_{11}–H and C_{14}–H). Found: C, 79.24; H, 10.28%. Calcd for $C_{20}H_{30}O_2$: C, 79.42; H, 10.00%. The physical and spectral data of **15b** were identical with those of the authentic (15*R*)-16-hydroxyferruginol.[4,5)]

Methyl (15*S*)-16-Benzoyloxy-12-hydroxy-8,11,13-abietatrien-18-oate (16a) and Its (15*R*)-Epimer (16b). a): A mixture of **8a** (1.412 g) and dilute hydrochloric acid (15%: 2.0 ml) in methanol (20 ml) was refluxed for 1 h. After removal of the methanol in vacuo, the residue was dissolved in ether and washed successively with brine, aqueous sodium hydrogencarbonate, and brine. The dried solution was evaporated in vacuo. The residue was chromatographed on silica gel (23 g), using ether–benzene (2:98) as an eluent, to give **16a** (1.123 g: 87.0%) as an oil, $[\alpha]_D$ +25.8° (*c* 3.96), IR 3600, 3400, and 1718 cm^{-1}; ^{1}H NMR δ=1.12 (3H, s, C_{10}–CH_3), 1.22 (3H, s, C_4–CH_3), 1.34 (3H, d, *J*=7 Hz, C_{15}–CH_3), 3.63 (3H, s, $-CO_2CH_3$), 3.9—4.7 (2H, m, C_{15}–CH_2O–), 6.62 (1H, s, overlap, C_{12}–OH), 6.62 (1H, s) and 6.71 (1H, s) (C_{11}–H and C_{14} –H), 7.2—7.6 (3H, m) and 7.99 (2H, dd, *J*=7 and 2 Hz) ($-OCOC_6H_5$). Found: C, 74.53; H, 7.67%. Calcd for $C_{28}H_{34}O_5$: C, 74.64; H, 7.61%.

b): A mixture of **8b** (308 mg) and dilute hydrochloric acid (15%: 0.4 ml) in methanol (4.0 ml) was refluxed for 1 h. After the work-up (as described in **a**)) the crude product was chromatographed on silica gel (8 g), using ether–benzene (1:99) as an eluent, to give **16b** (279 mg: 98.9%) which was recrystallized from acetone–hexane, mp 75—78 °C, [α]$_D$ +78.6 ° (*c* 2.10), IR 3600, 3400, and 1715 cm^{-1}, ^{1}H NMR δ=1.14 (3H, s, C$_{10}$–CH$_3$), 1.21 (3H, s, C$_4$–CH$_3$), 1.35 (3H, d, *J*=7 Hz, C$_{15}$–CH$_3$), 3.62 (3H, s, -CO$_2$CH$_3$), 3.8—4.7 (2H, m, C$_{15}$–CH$_2$O–), 6.20 (1H, s, C$_{12}$–OH), 6.59 (1H, s) and 6.69 (1H, s) (C$_{11}$–H and C$_{14}$–H), 7.2—7.6 (3H, m) and 8.03 (2H, dd, *J*=7 and 2 Hz) (-OCOC$_6$H$_5$). Found: C, 74.58; H, 7.83%. Calcd for C$_{28}$H$_{34}$O$_5$: C, 74.64; H, 7.61%.

Methyl (15*S*)-16-Benzoyloxy-12-(1-phenyl-1*H*-tetrazol-5-yloxy)-8,11,13-abietatrien-18-oate (17a) and Its (15*R*)-Epimer (17b). a): A stirred mixture of **16a** (980 mg), 5-chloro-1-phenyl-1*H*-tetrazole (97%: 810 mg), and anhydrous potassium carbonate (3.013 g) in ethyl methyl ketone (15 ml) was refluxed for 10 h. The mixture was cooled, diluted with water, and extracted with ether. The ether extract was washed with brine, dried, and evaporated in vacuo. The residue was chromatographed on silica gel (20 g), using hexane–benzene (1:3) and ether–benzene (5:95) as eluents, to give an oily **17a** (1.179 g: 91.1%), [α]$_D$ +61.1° (*c* 2.96), IR 1720 cm^{-1}, ^{1}H NMR (CDCl$_3$) δ=1.21 (3H, s) and 1.28 (3H, s) (C$_4$–CH$_3$ and C$_{10}$ –CH$_3$), 1.33 (3H, d, *J*=7 Hz, C$_{15}$–CH$_3$), 3.39 (1H, m, C$_{15}$–H), 3.67 (3H, s, -CO$_2$CH$_3$), 4.31 (2H, d, *J*=7 Hz, C$_{15}$–CH$_2$O–), 7.02 (1H, s, C$_{14}$–H), 7.22 (1H, s, C$_{11}$–H), 7.3—8.1 (10H, m, 2 -C$_6$H$_5$). Found: C, 70.98; H, 6.59; N, 9.42%. Calcd for C$_{35}$H$_{38}$O$_5$N$_4$: C, 70.68; H, 6.44; N, 9.42%.

b): A stirred mixture of **16b** (582 mg), 5-chloro-1-phenyl-1*H*-tetrazole (97%: 480 mg), and anhydrous potassium carbonate (1.785 g) in ethyl methyl ketone (10 ml) was refluxed for 10 h. After the work-up (as described in **a**)) the crude product was purified by column chromatography on silica gel (10 g), using benzene and ether–benzene (1:9) as eluents, to give an oily **17b** (726 mg: 94.6%), [α]$_D$ +45.4° (*c* 3.46), IR 1720 cm^{-1}, ^{1}H NMR (CDCl$_3$) δ=1.23 (3H, s) and 1.29 (3H, s) (C$_4$–CH$_3$ and C$_{10}$–CH$_3$), 1.33 (3H, d, *J*=7 Hz, C$_{15}$–CH$_3$), 3.39 (1H, m, C$_{15}$–H), 3.67 (3H, s, -CO$_2$CH$_3$), 4.31 (2H, d, *J*=7 Hz, C$_{15}$–CH$_2$O–), 7.04 (1H, s, C$_{14}$–H), 7.24 (1H, s, C$_{11}$–H), 7.3—8.1 (10H, m, 2 -C$_6$H$_5$). Found: C, 70.87; H, 6.38; N, 9.40%. Calcd for C$_{35}$H$_{38}$O$_5$N$_4$: C, 70.68; H, 6.44; N, 9.42%.

Hydrolyses of 17a and 17b. a): A mixture of **17a** (1.090 g), sodium carbonate (291 mg), water (4.0 ml), and methanol (40 ml) was stirred at room temperature for 2.5 h. The mixture was acidified with dilute hydrochloric acid and then evaporated in vacuo to remove most of the methanol. The residue was extracted with ether. The ether extract was washed successively with aqueous sodium hydrogencarbonate and brine, dried, and evaporated in vacuo. The residue was chromatographed on silica gel (30 g), using ether–benzene (8:92) as an eluent, to give the recovered **17a** (507 mg: 46.5%). Subsequent elution with ether–benzene (1:9) gave a 12,16-diol (74 mg: 11.7%, 21.8%[7]), the IR and ^{1}H NMR spectra of which were identical with those of the authentic **9a**. Further elution with ether–benzene (1:9 and then 3:7) afforded methyl (15*S*)-16-hydroxy-12-(1-phenyl-1*H*-tetrazol-5-yloxy)-8,11,13-abietatrien-18-oate (**18a**) as an oil (366 mg: 40.7%, 76.1%[7]), [α]$_D$ +34.0° (*c* 2.62), IR 3425 and 1720 cm^{-1}, ^{1}H NMR (90 MHz, CDCl$_3$) δ=1.18 (3H, d, *J*=7 Hz, C$_{15}$–CH$_3$), 1.19 (3H, s, C$_{10}$–CH$_3$), 1.25 (3H, s, C$_4$–CH$_3$), 3.11 (1H, m, C$_{15}$–H), 3.64 (2H, d, *J*=7 Hz, C$_{15}$–C$\underline{H}_2$OH), 3.66 (3H, s, -CO$_2$CH$_3$), 7.00 (1H, s, C$_{14}$–H), 7.16 (1H, s, C$_{11}$–H), 7.45—7.9 (5H, m, -C$_6$H$_5$). Found: C, 68.75; H, 7.26; N, 11.17%. Calcd for C$_{28}$H$_{34}$O$_4$N$_4$: C, 68.55; H, 6.99; N, 11.42%.

b): A mixture of **17b** (620 mg), sodium carbonate (166 mg), water (3.0 ml), and methanol (30 ml) was stirred at room temperature for 2 h. After the work-up (as described in **a**)) the crude product was chromatographed on silica gel (20 g), using ether–benzene (1:9) as an eluent, to give the recovered **17b** (306 mg: 49.4%) and a 12,16-diol (35 mg: 9.7%, 19.1%[7]), the IR and ^{1}H NMR spectra of which were identical with those of the authentic **9b**. Further elution with ether–benzene (1:9 and then 3:7) afforded methyl (15*R*)-16-hydroxy-12-(1-phenyl-1*H*-tetrazol-5-yloxy)-8,11,13-abietatrien-18-oate (**18b**) (200 mg: 39.1%, 77.2%[7]) which was recrystallized from acetone–hexane, mp 169—170 °C, [α]$_D$ +74.7° (*c* 1.78), IR 3425 and 1720 cm^{-1}, ^{1}H NMR (90 MHz, CDCl$_3$) δ=1.19 (3H, s, C$_{10}$–CH$_3$), 1.20 (3H, d, *J*=7 Hz, C$_{15}$–CH$_3$), 1.25 (3H, s, C$_4$–CH$_3$), 3.12 (1H, m, C$_{15}$–H), 3.64 (2H, d, *J*=7 Hz, C$_{15}$–C$\underline{H}_2$OH), 3.66 (3H, s. -CO$_2$CH$_3$), 7.00 (1H, s, C$_{14}$–H), 7.16 (1H, s, C$_{11}$–H), 7.45—7.9 (5H, m, -C$_6$H$_5$). Found: C, 68.36; H, 7.18; N, 11.44%. Calcd for C$_{28}$H$_{34}$O$_4$N$_4$: C, 68.55; H, 6.99; N, 11.42%.

Reactions of 9a and 9b with 5-Chloro-1-phenyl-1*H*-tetrazole. a): A stirred mixture of **9a** (145 mg), 5-chloro-1-phenyl-1*H*-tetrazole (97%: 156 mg), and anhydrous potassium carbonate (579 mg) in ethyl methyl ketone (5.0 ml) was refluxed for 10 h. After the work-up (as described above) the crude product was chromatographed on silica gel (8 g), using hexane–benzene (2:3) as an eluent, to give a dihydrobenzofuran derivative (51.3 mg: 37.3%) which was identical with authentic methyl (15*S*)-12,16-epoxy-8,11,13-abietatrien-18-oate (**19a**).[6] ^{1}H NMR (90 MHz, CDCl$_3$) δ=1.18 (3H, s, C$_{10}$–CH$_3$), 1.25 (3H, s, C$_4$–CH$_3$), 1.28 (3H, d, *J*=7 Hz, C$_{15}$–CH$_3$), 3.47 (1H, m, C$_{15}$–H), 3.66 (3H, s, -CO$_2$CH$_3$), 3.99 (1H, dd, *J*=8 and 7 Hz) and 4.62 (1H, t, *J*=8 Hz) (C$_{15}$–CH$_2$O–), 6.67 (1H, s, C$_{11}$–H), 6.78 (1H, s, C$_{14}$–H). Further elution with ether–benzene (15:85) afforded **18a** (98.5 mg: 48.0%), the IR and ^{1}H NMR spectra of which were identical with those of the authentic sample.

b): A stirred mixture of **9b** (67.8 mg), 5-chloro-1-phenyl-1*H*-tetrazole (97%: 70.8 mg), and anhydrous potassium carbonate (271 mg) in ethyl methyl ketone (3.0 ml) was refluxed for 10 h. After the work-up (as described above) the crude product was chromatographed on silica gel (12 g), using hexane–benzene (1:3) as an eluent, to give a dihydrobenzofuran derivative (24.2 mg: 37.6%) which was identical with authentic methyl (15*R*)-12,16-epoxy-8,11,13-abietatrien-18-oate (**19b**).[6] ^{1}H NMR (90 MHz, CDCl$_3$) δ=1.18 (3H, s, C$_{10}$–CH$_3$), 1.25 (3H, s, C$_4$–CH$_3$), 1.27 (3H, d, *J*=7 Hz, C$_{15}$–CH$_3$), 3.47 (1H, m, C$_{15}$–H), 3.66 (3H, s, -CO$_2$CH$_3$), 4.00 (1H, dd, *J*=*8* and 7 Hz) and 4.62 (1H, t, *J*=8 Hz) (C$_{15}$–CH$_2$O–), 6.68 (1H, s, C$_{11}$–H), 6.80 (1H, s, C$_{14}$–H). Further elution with ether–benzene (1:4) afforded **18b** (28.5 mg: 29.6%), mp 169—170 °C (from acetone–hexane), the IR and ^{1}H NMR spectra of which were identical with those of the authentic sample.

Methyl (15*S*)-16-Hydroxy-8,11,13-abietatrien-18-oate (3a) and Its (15*R*)-Epimer (3b). a): A mixture of **18a** (219.0 mg) and 10% Pd-C (300 mg) in ethanol (15 ml) was hydrogenated at room temperature under an atmosphere of hydrogen for 85 h. After the usual work-up, the crude product was chromatographed on silica gel (10 g), using ether-benzene (5:95) as an eluent, to give an oily **3a** (37.6 mg: 25.5%, 39.3%[7]) which was allowed to stand at room temperature to give a solid, mp 51—53.5 °C, $[\alpha]_D$ +44.7° (*c* 1.37). IR 3590, 3475, and 1718 cm^{-1}; ^{1}H NMR (90 MHz) δ=1.16 (3H, s, C_{10}-CH_3), 1.17 (3H, d, *J*=7 Hz, C_{15}-CH_3), 1.22 (3H, s, C_4-CH_3), 1.39 (1H, s, C_{16}-OH), 3.50 (2H, d, *J*=7 Hz, C_{15}-$C\underline{H}_2OH$), 3.60 (3H, s, -CO_2CH_3), 6.77 (1H, bs, C_{14}-H), 6.84 (1H, dd, *J*=8 and 2 Hz, C_{12}-H), 7.07 (1H, d, *J*=8 Hz, C_{11}-H). Found: C, 76.18; H, 9.03%. Calcd for $C_{21}H_{30}O_3$: C, 76.32; H, 9.15%. Further elution with ether-benzene (1:9) afforded a 12,16-diol **9a** (21.6 mg: 14.0%, 21.6%[7]), and the recovered **18a** (77.1 mg: 35.2%).

b): A mixture of **18b** (105.0 mg) and 10% Pd-C (110 mg) in ethanol (7.0 ml) was hydrogenated at room temperature under an atmosphere of hydrogen for 64 h. After the usual work-up, the crude product was chromatographed on silica gel (8 g), using ether-benzene (1:9) as an eluent, to give **3b** (64.6 mg: 91.4%) which was recrystallized from hexane, mp 71.5—73 °C, $[\alpha]_D$ +65.8 ° (*c* 1.57), IR 3590, 3475, and 1718 cm^{-1}; ^{1}H NMR (90 MHz) δ=1.16 (3H, s, C_{10}-CH_3), 1.17 (3H, d, *J*=7 Hz, C_{15}-CH_3), 1.22 (3H, s, C_4-CH_3), 1.32 (1H, s, C_{16}-OH), 3.50 (2H, d, *J*=7 Hz, C_{15}-$C\underline{H}_2OH$), 3.60 (3H, s, -CO_2CH_3), 6.77 (1H, bs, C_{14}-H), 6.84 (1H, dd, *J*=8 and 2 Hz, C_{12}-H), 7.07 (1H, d, *J*=8 Hz, C_{11}-H). Found: C, 76.21; H, 9.33%. Calcd for $C_{21}H_{30}O_3$: C, 76.32; H, 9.15%.

Methyl (15*S*)-16-(4-Nitrobenzoyloxy)-8,11,13-abietatrien-18-oate (20a) and Its (15*R*)-Epimer (20b). a): A mixture of **3a** (25.0 mg) and 4-nitrobenzoyl chloride (28.1 mg) in pyridine (1.0 ml) was heated at 70—80 °C for 2.5 h. After the usual work-up, the crude product was chromatographed on silica gel (8 g), using benzene as an eluent, to give **20a** (35.0 mg: 96.5%) which was recrystallized from hexane, mp 116—117 °C, $[\alpha]_D$ +9.2 ° (*c* 2.95), IR 1720, 1530, and 1350 cm^{-1}; ^{1}H NMR (90 MHz, $CDCl_3$) δ=1.18 (3H, s, C_{10}-CH_3), 1.26 (3H, s, C_4-CH_3), 1.35 (3H, d, *J*=7 Hz, C_{15}-CH_3), 3.18 (1H, m, C_{15}-H), 3.67 (3H, s, -CO_2CH_3), 4.41 (2H, d, *J*=7 Hz, C_{15}-CH_2O-), 6.90 (1H, bs, C_{14}-H), 7.01 (1H, dd, *J*=8 and 2 Hz, C_{12}-H), 7.20 (1H, d, *J*=8 Hz, C_{11}-H), 8.10 (2H, d, *J*=8 Hz) and 8.28 (2H, d, *J*=8 Hz) (-$C_6H_4NO_2$). Found: C, 70.34; H, 7.17; N, 2.62%. Calcd for $C_{28}H_{33}O_6N$: C, 70.12; H, 6.94; N, 2.92%.

b): A mixture of **3b** (38.0 mg) and 4-nitrobenzoyl chloride (42.7 mg) in pyridine (1.5 ml) was heated at 70—80°C for 2.5 h. After the usual work-up, the crude product was chromatographed on silica gel (6 g), using benzene as an eluent, to give **20b** (53.3 mg: 96.7%) which was recrystallized from hexane, mp 133—134 °C, $[\alpha]_D$ +66.4 ° (*c* 2.23), IR 1720, 1530, and 1350 cm^{-1}; ^{1}H NMR (90 MHz, $CDCl_3$) δ=1.18 (3H, s, C_{10}-CH_3), 1.26 (3H, s, C_4-CH_3), 1.36 (3H, d, *J*=7 Hz, C_{15}-CH_3), 3.18 (1H, m, C_{15}-H), 3.67 (3H, s, -CO_2CH_3), 4.41 (2H. d, *J*=7 Hz, C_{15}-CH_2O-), 6.90 (1H, bs, C_{14}-H), 7.01 (1H, dd, *J*=8 and 2 Hz, C_{12}-H), 7.20 (1H, d, *J*=8 Hz, C_{11}-H), 8.10 (2H, d, *J*=8 Hz) and 8.28 (2H, d, *J*=8 Hz) (-$C_6H_4NO_2$). Found: C, 70.38; H, 7.14; N, 2.93%. Calcd for $C_{28}H_{33}O_6N$: C, 70.12; H, 6.94; N, 2.92%.

c): Methyl (+)-16-hydroxydehydroabietate[2] (20.0 mg) ($[\alpha]_D$ +48.6° (*c* 1.11)[8]), a methyl ester of a metabolite of (+)-dehydroabietic acid (**2**) in rabbits, was treated with 4-nitrobenzoyl chloride (23.0 mg) in pyridine (1.5 ml) at 70—80°C for 2.5 h. After the usual work-up, the crude product was chromatographed on silica gel (7 g), using benzene as an eluent, to give a 4-nitrobenzoate (28.7 mg: 99.0%) which was recrystallized from hexane, mp 116—117°C, $[\alpha]_D$ +9.5 ° (*c* 1.16), IR 1720, 1530, and 1350 cm^{-1}; ^{1}H NMR (90 MHz, $CDCl_3$) δ=1.18 (3H, s, C_{10}-CH_3), 1.26 (3H, s, C_4-CH_3), 1.35 (3H, d, *J*=7 Hz, C_{15}-CH_3), 3.18 (1H, m, C_{15}-H), 3.67 (3H, s, -CO_2CH_3), 4.41 (2H, d, *J*=7 Hz, C_{15}-CH_2O-), 6.90 (1H, bs, C_{14}-H), 7.01 (1H, dd, *J*=8 and 2 Hz, C_{12}-H), 7.20 (1H, d, *J*=8 Hz, C_{11}-H), 8.10 (2H, d, *J*=8 Hz) and 8.28 (2H, d, *J*=8 Hz) (-$C_6H_4NO_2$). Found: C, 70.37; H, 7.15; N, 2.76%. Calcd for $C_{28}H_{33}O_6N$: C, 70.12; H, 6.94; N, 2.92%.

The physical and spectral data of the natural 4-nitrobenzoate were identical with those of the synthetic (15*S*)-isomer **20a**.

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7) Yields are based on the starting material consumed.

8) The optical rotation was measured in our laboratory.