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The Synthesis of Lycoxanthol and Its C-15 Epimer

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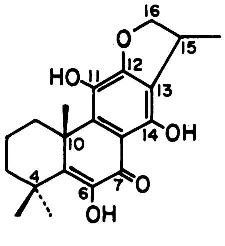
In order to elucidate the absolute configuration of C-15 in natural lycoxanthol, (15*R*)-11,16-dihydroxy-12-methoxymethoxy-8,11,13-abietatrien-7-one and its (15*S*)-epimer were transformed into (15*R*)-12,16-epoxy-6,11,14-trihydroxy-5,8,11,13-abietatetraen-7-one (**1a**) and its (15*S*)-epimer, respectively. The synthetic **1a** was identical with natural lycoxanthol. Thus, the stereochemistry of C-15 in the natural compound was conclusively assigned as R-configuration.

Lycoxanthol, a highly oxygenated abietane-type diterpene possessing a dihydrofuran moiety, has been isolated from *Lycopodium lucidulum* by Burnell et al.[1,2] On the basis of chemical and spectroscopic studies, they deduced the structure of lycoxanthol to be 12,16-epoxy-6,11,14-trihydroxy-5,8,11,13-abietatetraen-7-one (**1**). However, the absolute configuration of C-15 in the natural compound remained unsettled. In order to elucidate the unknown stereochemistry at C-15, we have now attempted the syntheses of (15*R*)-12,16-epoxy-6,11,14-trihydroxy-5,8,11,13-abietatetraen-7-one (**1a**) and its (15*S*)-epimer (**1b**). For this purpose, (15*R*)-11,16-dihydroxy-12-methoxymethoxy-8,11,13-abietatrien-7-one (**2a**)[3] and its (15*S*)-epimer (**2b**)[3] were chosen as convenient relay intermediates, because these compounds have recently been synthesized in our laboratory by an unambiguous method starting from (+)-dehydroabietic acid.



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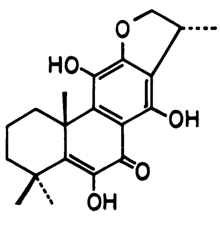
Mesylation of the 12-methoxymethyl ether **2a** with methanesulfonyl chloride in pyridine afforded a mesylate **3a** which was converted into 12,16-epoxy-11-hydroxy-8,11,13-abietatrien-7-one (**4a**) by refluxing with sodium iodide in ethyl methyl ketone and then with anhydrous potassium carbonate in ethyl methyl ketone in 87.2% yield from **2a**. The ^{1}H NMR spectrum of **4a** showed signals at δ 1.30 (3H, doublet), ca. 3.5 (1H, multiplet), 4.13 (1H, double doublet), and 4.75 ppm (1H, triplet) due to a dihydrofuran moiety. For the protection of the hydroxyl group, the dihydrobenzofuran derivative **4a** was acetylated with acetic anhydride in pyridine to give an acetate **5a** in 95.0% yield. This was reduced with sodium borohydride in a mixture of ether and methanol at room temperature, and the resulting crude product was immediately refluxed with *p*-toluenesulfonic acid in benzene to give 11-acetoxy-12,16-epoxy-6,8,11,13-abietatetraene (**6a**) in 93.1% yield. Epoxidation of **6a** with *m*-chloroperbenzoic acid in dichloromethane followed by treatment with *p*-toluenesulfonic acid in refluxing benzene afforded 11-acetoxy-12,16-epoxy-8,11,13-abietatrien-6-one (**7a**) in 63.1% yield. To introduce an oxygen function at the C-14 position, the 6-oxo compound **7a** was reduced with lithium aluminium hydride in ether and the resulting 6*β*,11-diol (**8a**: 94.5%) was then oxidized with *m*-chloroperbenzoic acid in tetrahydrofuran at room temperature to give a *p*-quinone, 12,16-epoxy-6*β*-hydroxy-8,12-abietadiene-11,14-dione (**9a**) in 19% yield.[4] In the ^{1}H NMR spectrum of **8a**, the downfield shift of a signal (δ 1.70) due to the methyl group at C-10 relative to the corresponding signal (δ 1.33) for **7a** suggested a 1,3-diaxial-*cis*-relationship between the methyl group and the hydroxyl group at C-6. For the protection of the *p*-quinone moiety, the hydroxy quinone **9a** was subjected to reductive acetylation with zinc powder and acetic anhydride in pyridine, and the resulting crude product was immediately oxidized with Jones reagent at 0—5 °C to give 11,14-diacetoxy-12,16-epoxy-8,11,13-abietatrien-6-one (**10a**) in 20% yield. To introduce a final oxygen function at the C-7 position, the diacetate **10a** was further oxidized with Jones reagent at room temperature and the crude product, without purification, was hydrolyzed with dilute hydrochloric acid in refluxing ethanol to give the desired (15*R*)-12,16-epoxy-6,11,14-trihydroxy-5,8,11,13-abietatetraen-7-one (**1a**), mp 250—251 °C, in 31% yield. The synthetic **1a** was identical with natural lycoxanthol (mp 249 °C).

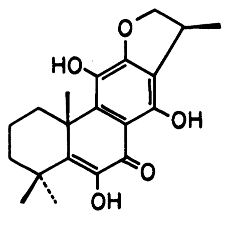
For direct comparison with **1a**, the synthesis of (15*S*)-12,16-epoxy-6,11,14-trihydroxy-5,8,11,13-abietatetraen-7-one (**1b**) was also carried out in the same manner to that described for the preparation of **1a**. Mesylation of (15*S*)-11,16-dihydroxy-12-methoxymethoxy-8,11,13-abietatrien-7-one (**2b**) with methanesulfonyl chloride in pyridine, followed by treatment of the resulting mesylate **3b** with sodium iodide in refluxing ethyl methyl ketone and then with anhydrous potassium carbonate in refluxing ethyl methyl ketone afforded 12,16-epoxy-11-hydroxy-8,11,13-abietatrien-7-one (**4b**) in 97.8% yield from **2b**. The 11-

hydroxy compound **4b** was acetylated with acetic anhydride in pyridine and the acetate (**5b**: 94.8%) was then transformed into 11-acetoxy-12,16-epoxy-6,8,11,13-abietatetraene (**6b**: 83.0%) by sodium borohydride reduction and acid-catalyzed dehydration. Oxidation of **6b** with *m*-chloroperbenzoic acid followed by treatment with *p*-toluenesulfonic acid led to 11-acetoxy-12,16-epoxy-8,11,13-abietatrien-6-one (**7b**) in 58.0% yield. This was reduced with lithium aluminium hydride to give the corresponding 6β,11-diol (**8b**: 99.2%) which was then converted into 12,16-epoxy-6β-hydroxy-8,12-abietadiene-11,14-dione (**9b**: 16.4%[4]) by oxidation with *m*-chloroperbenzoic acid. Reductive acetylation of **9b** with zinc powder and acetic anhydride in pyridine, followed by oxidation with Jones reagent at 0—5 °C produced 11,14-diacetoxy-12,16-epoxy-8,11,13-abietatrien-6-one (**10b**) in 28.7% yield. Further oxidation of **10b** with Jones reagent at room temperature and subsequent hydrolysis with dilute hydrochloric acid afforded the desired **1b** (40%), mp 219—220 °C, which was not identical with natural lycoxanthol.

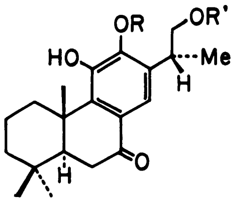
From the present study, the stereochemistry of C-15 in natural lycoxanthol was conclusively assigned as R-configuration.

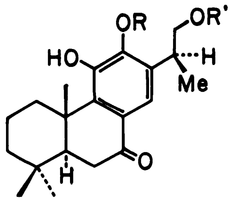


1a

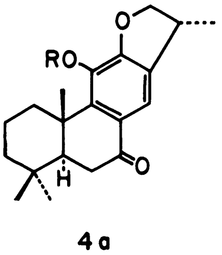


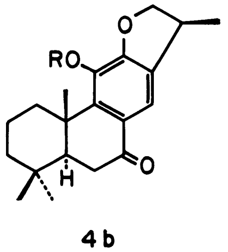
1b



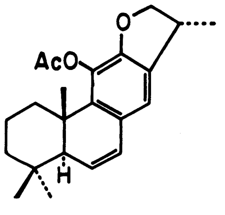


2a R=CH$_2$OMe, R'=H 2b
3a R=CH$_2$OMe, R'=Ms 3b

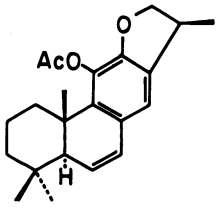




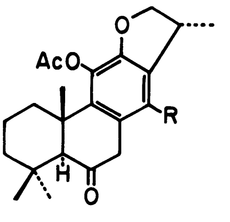
4a R=H 4b
5a R=Ac 5b

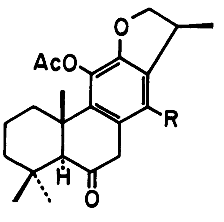


6a

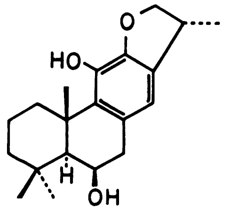


6b

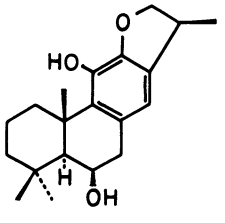




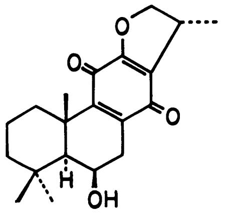
7a R=H 7b
10a R=OAc 10b



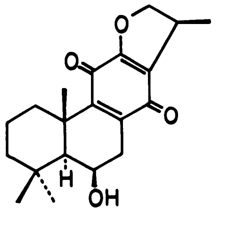
8a



8b



9a



9b

Experimental

All melting points are uncorrected. The IR spectra and optical rotations were measured in chloroform, and the ^{1}H NMR spectra in deuteriochloroform 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, t: triplet, m: multiplet. The column chromatography was performed using Merck silica gel (0.063 mm).

(15*R*)-12,16-Epoxy-11-hydroxy-8,11,13-abietatrien-7-one (4a) and Its (15*S*)-Epimer (4b). a) A mixture of (15*R*)-11,16-dihydroxy-12-methoxymethoxy-8,11,13-abietatrien-7-one (**2a**)[3] (4.485 g) and methanesulfonyl chloride (1.1 ml) in pyridine (10 ml) was allowed to stand at room temperature for 15 h and then poured into a mixture of ice and dilute hydrochloric acid. The mixture was extracted with ether.

The ether extract was washed with brine, dried over sodium sulfate, and evaporated in vacuo to give a crude mesylate (**3a**), IR 3490—3325, 1670, 1360, and 1170 cm^{-1}; ^{1}H NMR δ=0.95 (3H, s) and 0.98 (3H, s) ($-\overset{|}{C}(CH_3)_2$), 1.32 (3H, d, *J*=7 Hz, C_{15}-CH_3), 1.41 (3H, s, C_{10}-CH_3), 2.91 (3H, s, $-OSO_2CH_3$), 3.67 (3H, s, $-OCH_3$), 4.22 (2H, bd, *J*=7 Hz, $-C\underline{H}_2OSO_2CH_3$), 5.03 (2H, s, $-OCH_2O-$), 7.45 (1H, s) and 7.51 (1H, s) (C_{11}-OH and C_{14}-H).

A stirred mixture of the above crude **3a** and sodium iodide (3.572 g) in ethyl methyl ketone (40 ml) was refluxed for 4 h. After cooling, the mixture was poured into water and extracted with ether. The ether extract was washed successively with aqueous sodium thiosulfate and brine. The dried solution was evaporated in vacuo. The residue was further refluxed with anhydrous potassium carbonate (3.5 g) in ethyl methyl ketone (20 ml) for 2.5 h. After cooling, the mixture 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 crude product was purified by column chromatography on silica gel (100 g), using ether-benzene (1 : 99) as eluent, to give an oily **4a** (3.268 g: 87.2% yield from **2a**), $[\alpha]_D$ +17.1° (*c* 12.35), IR 3560, 3320, and 1668 cm^{-1}; ^{1}H NMR δ=0.94 (3H, s) and 0.97 (3H, s) ($-\overset{|}{C}(CH_3)_2$), 1.30 (3H, d, *J*=7 Hz, C_{15}-CH_3), 1.39 (3H, s, C_{10}-CH_3), ca. 3.5 (1H, m, C_{15}-H), 4.13 (1H, dd, *J*=7 and 8 Hz) and 4.75 (1H, t, *J*=7 Hz) ($-OCH_2-$), 5.36 (1H, s, C_{11}-OH), 7.60 (1H, bs, C_{14}-H). Found: C, 76.54; H, 8.64%. Calcd for $C_{20}H_{26}O_3$: C, 76.40; H, 8.34%.

b): A mixture of (15*S*)-11,16-dihydroxy-12-methoxymethoxy-8,11,13-abietatrien-7-one (**2b**)[3] (4.104 g) and methanesulfonyl chloride (0.93 ml) in pyridine (10 ml) was treated as described in **a**) to give a crude mesylate **3b**, IR 3490—3325, 1678, 1360, and 1170 cm^{-1}; ^{1}H NMR δ=0.96 (3H, s) and 0.99 (3H, s) ($-\overset{|}{C}(CH_3)_2$), 1.29 (3H, d, *J*=7 Hz, C_{15}-CH_3), 1.42 (3H, s, C_{10}-CH_3), 2.93 (3H, s, $-OSO_2CH_3$), 3.68 (3H, s, $-OCH_3$), 4.26 (2H, bd, *J*=7 Hz, $-C\underline{H}_2OSO_2CH_3$), 5.04 (2H, s, $-OCH_2O-$), 7.48 (1H, s) and 7.53 (1H, s) (C_{11}-OH and C_{14}-H).

A stirred mixture of the above crude **3b** and sodium iodide (3.268 g) in ethyl methyl ketone (40 ml) was refluxed for 4 h. After the work-up as described in **a**), the crude product was further refluxed with anhydrous potassium carbonate (3.0 g) in ethyl methyl ketone (20 ml) for 2.5 h. The crude product was purified by column chromatography on silica gel (100 g), using ether-benzene (1 : 99) as eluent, to give an oily **4b** (3.352 g: 97.8% yield from **2b**), $[\alpha]_D$ +33.3° (*c* 8.95), IR 3560, 3320, and 1669 cm^{-1}; ^{1}H NMR δ=0.95 (3H, s) and 0.97 (3H, s) ($-\overset{|}{C}(CH_3)_2$), 1.33 (3H, d, *J*=7 Hz, C_{15}-CH_3), 1.40 (3H, s, C_{10}-CH_3), *ca.* 3.5 (1H, m, C_{15}-H), 4.14 (1H, dd, *J*=7 and 8 Hz) and 4.78 (1H, t, *J*=8 Hz) ($-OCH_2-$), 5.33 (1H, s, C_{11}-OH), 7.62 (1H, bs, C_{14}-H). Found: C, 76.13; H, 8.54%. Calcd for $C_{20}H_{26}O_3$: C, 76.40; H, 8.34%.

(15*R*)-11-Acetoxy-12,16-epoxy-8,11,13-abietatrien-7-one (5a) and Its (15*S*)-Epimer (5b). **a)**: A mixture of **4a** (1.403 g) and acetic anhydride (3.0 ml) in pyridine (4.0 ml) was heated at 75—80 °C for 2.5 h. After the usual work-up, the crude product was chromatographed on silica gel (50 g), using ether-benzene (1 : 99 and then 5 : 95) as eluents, to give **5a** (1.511 g: 95.0%) which was recrystallized from hexane, mp 165—166.5 °C, IR 1770 and 1668 cm^{-1}, ^{1}H NMR δ=0.94 (3H, s) and 0.97 (3H, s) ($-\overset{|}{C}(CH_3)_2$), 1.32 (3H, d, *J*=7 Hz, C_{15}-CH_3), 1.33 (3H, s, C_{10}-CH_3), 2.32 (3H, s, $-OCOCH_3$), ca. 3.5 (1H, m, C_{15}-H), 4.13 (1H, dd, *J*=7 and 9 Hz) and 4.73 (1H, t, *J*=9 Hz) ($-OCH_2-$), 7.88 (1H, d, *J*=1 Hz, C_{14}-H). Found: C, 74.33 H, 8.18%. Calcd for $C_{22}H_{28}O_4$: C, 74.13; H, 7.92%.

b): A mixture of **4b** (3.047 g) and acetic anhydride (7.0 ml) in pyridine (7.0 ml) was heated at 75—80 °C for 2 h. After the usual work-up, the crude product was chromatographed on silica gel (100 g), using ether-benzene (1 : 99 and then 5 : 95) as eluents, to give **5b** (3.273 g: 94.8%) which was recrystallized from hexane, mp 156.5—158 °C, $[\alpha]_D$ +64.4° (*c* 4.64), IR 1770 and 1668 cm^{-1}, ^{1}H NMR δ=0.99 (6H, s, $-\overset{|}{C}(CH_3)_2$), 1.36 (3H, s, C_{10}-CH_3), 1.36 (3H, d, *J*=7 Hz, C_{15}-CH_3), 2.33 (3H, s, $-OCOCH_3$), *ca.* 3.5 (1H, m, C_{15}-H), 4.12 (1H, dd, *J*=7 and 9 Hz) and 4.79 (1H, t, *J*=9 Hz) ($-OCH_2-$), 7.91 (1H, d, *J*=1 Hz, C_{14}-H). Found: C, 74.26; H, 8.17%. Calcd for $C_{22}H_{28}O_4$: C, 74.13; H, 7.92%.

(15*R*)-11-Acetoxy-12,16-epoxy-6,8,11,13-abietatetraene (6a) and Its (15*S*)-Epimer (6b). **a)**: A suspension of **5a** (648 mg) and sodium borohydride (69 mg) in ether-methanol (2 : 1) (9.0 ml) was stirred at 0—5 °C for 15 min and at room temperature for 1 h. The mixture was acidified with dilute hydrochloric acid and extracted with ether. The ether extract was washed with brine, dried, and evaporated in vacuo. The residue was refluxed with *p*-toluenesulfonic acid (50 mg) in dry benzene (10 ml) for 1 h, cooled, and diluted with ether. The ether solution was washed with water, dried, and evaporated in vacuo. The crude product was chromatographed on silica gel (50 g), using benzene as eluent, to give an oily **6a** (576 mg: 93.1%), $[\alpha]_D$ −55.9° (*c* 1.67), IR 1750 cm^{-1}, ^{1}H NMR δ=0.95 (3H, s), 1.01 (3H, s), and 1.10 (3H, s) ($-\overset{|}{C}(CH_3)_2$ and C_{10}-CH_3), 1.27 (3H, d, *J*=6.5 Hz, C_{15}-CH_3), 2.28 (3H, s, $-OCOCH_3$), ca. 3.5 (1H, m, C_{15}-H), 4.03 (1H, dd, *J*=7 and 9 Hz) and 4.63 (1H, t, *J*=9 Hz) ($-OCH_2-$), 5.79 (1H, dd, *J*=3 and 9.5 Hz, C_6-H), 6.42 (1H, dd, *J*=3 and 9.5 Hz, C_7-H), 6.72 (1H, s, C_{14}-H). Found: C, 77.91; H, 8.56%. Calcd for $C_{22}H_{28}O_3$: C, 77.61; H, 8.29%

b): A suspension of **5b** (3.273 g) and sodium borohydride (348 mg) in ether-methanol (2 : 1) (15 ml) was stirred at 0—5 °C for 15 min and at room temperature for 2 h. After the work-up as described in **a**), the crude product was refluxed with *p*-toluenesulfonic acid (200 mg) in dry benzene (30 ml) for 1 h. The mixture was cooled and diluted with ether. The ether solution was washed with water, dried, and evaporated in vacuo. The residue was chromatographed on silica gel (60 g), using benzene as eluent, to give an oily **6b** (2.594 g: 83.0%), $[\alpha]_D$ −102.8° (*c* 6.48), IR 1752 cm^{-1}, ^{1}H NMR δ=0.96 (3H, s), 1.01 (3H, s), and 1.11 (3H, s) ($-\overset{|}{C}(CH_3)_2$ and C_{10}-CH_3), 1.30 (3H, d, *J*=6.5 Hz, C_{15}-CH_3), 2.29 (3H, s, $-OCOCH_3$), ca. 3.5 (1H, m, C_{15}-H), 4.02 (1H, t, *J*=9 Hz) and 4.69 (1H, t, *J*=9 Hz) ($-OCH_2-$), 5.81 (1H, dd, *J*=3 and 9.5 Hz, C_6-H), 6.44 (1H, dd, *J*=3 and 9.5 Hz, C_7-H), 6.72 (1H, s, C_{14}-H). Found: C, 77.41; H, 8.52%. Calcd for $C_{22}H_{28}O_3$: C, 77.61; H, 8.29%.

(15*R*)-11-Acetoxy-12,16-epoxy-8,11,13-abietatrien-6-one (7a) and Its (15*S*)-Epimer (7b). **a)**: A mixture of **6a** (508 mg) and *m*-chloroperbenzoic acid (80%: 483 mg) in dichloromethane (5.0 ml) was stirred at 0—5 °C for 30 min and at room temperature for 17 h. The mixture was diluted with ether and washed successively with aqueous potassium iodide, aqueous sodium thiosulfate, aqueous sodium hydrogencarbonate, and brine. The dried solution was evaporated in vacuo. The residual oil was refluxed with *p*-toluenesulfonic acid (50 mg) in dry benzene (5.0 ml) for 1 h, cooled, and diluted with ether. The ether solution was washed successively with water, aqueous sodium hydrogencarbonate, and water. The dried solution was evaporated in vacuo. The crude product was chromatographed on silica gel (50 g), using ether-benzene (1 : 99) as eluent, to give an oily **7a** (332 mg: 63.1%), $[\alpha]_D$ +44.8° (c 4.58), IR 1763 and 1716cm^{-1}, ^{1}H NMR δ=1.03 (3H, s) and 1.22 (3H, s) ($-\overset{|}{C}(CH_3)_2$), 1.29 (3H, d, J=7 Hz, C_{15}-CH_3), 1.33 (3H, s, C_{10}-CH_3), 2.32 (3H, s, -$OCOCH_3$), 2.60 (1H, s, C_5-H), 3.34 (1H, bd, J=21 Hz) and 3.76 (1H, d, J=21 Hz) (-$COCH_2$-), 4.08 (1H, dd, J=7 and 9 Hz) and 4.67 (1H, t, J=9 Hz) (-OCH_2-), 6.72 (1H, s, C_{14}-H). Found: C, 73.92; H, 8.09%. Calcd for $C_{22}H_{28}O_4$: C, 74.13; H, 7.92%.

b): A mixture of **6b** (2.820 g) and m-chloroperbenzoic acid (80%: 2.680 g) in dichloromethane (20 ml) was stirred at 0—5 °C for 30 min and at room temperature for 13 h. After the work-up as described in **a**), the crude product was refluxed with p-toluenesulfonic acid (100 mg) in dry benzene (20 ml) for 1 h. The mixture was cooled, diluted with ether, and washed successively with water, aqueous sodium hydrogencarbonate, and water. The dried solution was evaporated in vacuo. The residue was chromatographed on silica gel (50 g), using ether-benzene (1 : 99) as eluent, to give an oily **7b** (1.712 g: 58.0%), $[\alpha]_D$ +54.6° (c 6.54), IR 1761 and 1712 cm^{-1}, ^{1}H NMR δ=1.02 (3H, s) and 1.22 (3H, s) ($-\overset{|}{C}(CH_3)_2$), 1.29 (3H, d, J=7 Hz, C_{15}-CH_3), 1.31 (3H, s, C_{10}-CH_3), 2.28 (3H, s, -$OCOCH_3$), 2.55 (1H, s, C_5-H), 3.31 (1H, d, J=21 Hz) and 3.71 (1H, d, J=21 Hz) (-$COCH_2$-), 4.00 (1H, t, J=8 Hz) and 4.68 (1H, t, J=8 Hz) (-OCH_2-), 6.66 (1H, s, C_{14}-H). Found: C, 74.26; H, 7.79%. Calcd for $C_{22}H_{28}O_4$: C, 74.13; H, 7.92%.

(15*R*)-12,16-Epoxy-8,11,13-abietatriene-6*β*,11-diol (8a) and Its (15*S*)-Epimer (8b). **a**): A mixture of **7a** (434.0 mg) and lithium aluminium hydride (69.3 mg) in dry ether (7.0 ml) was refluxed for 1.5 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 **8a** as a solid (364.3 mg: 94.5%) which was recrystallized from acetone-hexane, mp 216—218 °C, IR (KBr) 3580 and 3380 cm^{-1}, ^{1}H NMR δ=1.03 (3H, s) and 1.27 (3H, s) ($-\overset{|}{C}(CH_3)_2$), 1.28 (3H, d, J=7 Hz, C_{15}-CH_3), 1.70 (3H, s, C_{10}-CH_3), 4.02 (1H, t, J=8 Hz) and 4.63 (1H, t, J=8 Hz) (-OCH_2-), 4.55 (1H, overlap, C_6-H), 5.03 (1H, s, C_{11}-OH), 6.42 (1H, s, C_{14}-H). Found: C, 76.16; H, 9.13%. Calcd for $C_{20}H_{28}O_3$: C, 75.91; H, 8.92%.

b): A mixture of **7b** (1.252 g) and lithium aluminium hydride (133 mg) in dry ether (10 ml) was refluxed for 1.5 h to give a crude **8b** as a solid (1.102 g: 99.2%). This was recrystallized from acetone-hexane, mp 212—214.5 °C, IR (KBr) 3490 and 3230 cm^{-1} ^{1}H NMR δ=1.03 (3H, s) and 1.27 (3H, s) ($-\overset{|}{C}(CH_3)_2$), 1.27 (3H, d, J=7 Hz, C_{15}-CH_3), 1.70 (3H, s, C_{10}-CH_3), 4.00 (1H, t, J=8 Hz) and 4.66 (1H, t, J=8 Hz) (-OCH_2-), 4.55 (1H, overlap, C_6-H), 5.01 (1H, s, C_{11}-OH), 6.42 (1H, s, C_{14}-H). Found: C, 76.20; H, 9.15%. Calcd for $C_{20}H_{28}O_3$: C, 75.91; H, 8.92%.

(15*R*)-12,16-Epoxy-6*β*-hydroxy-8,12-abietadiene-11,14-dione (9a) and Its (15*S*)-Epimer (9b). **a**): A mixture of the above crude **8a** (56.2 mg) and m-chloroperbenzoic acid (80%: 42.1 mg) in tetrahydrofuran (2.0 ml) was stirred at room temperature for 18 h. The mixture was diluted with ether and 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 (7.0 g), using chloroform as eluent, to give the starting **8a** (19.1 mg) and a p-quinone **9a** (7.2 mg: 12%). The p-quinone **9a** was recrystallized from acetone-hexane, mp 224—225 °C, $[\alpha]_D$ +39° (c 0.51), IR 3620, 3530, 1669sh, 1652, and 1636 cm^{-1}; ^{1}H NMR δ=1.00 (3H, s) and 1.25 (3H, s) ($-\overset{|}{C}(CH_3)_2$), 1.29 (3H, d, J=7 Hz, C_{15}-CH_3), 1.63 (3H, s, C_{10}-CH_3), 4.17 (1H, dd, J=6 and 9.5 Hz) and 4.72 (1H, t, J=9.5 Hz) (-OCH_2-), ca. 4.6 (1H, overlap, C_6-H). Found: C, 72.47; H, 7.69%. Calcd for $C_{20}H_{26}O_4$: C, 72.70; H, 7.93%.

b): A mixture of the crude **8b** (880 mg) and m-chloroperbenzoic acid (80%: 660 mg) in tetrahydrofuran (5.0 ml) was stirred at room temperature for 17.5 h. After the work-up as described in **a**), the crude product was chromatographed on silica gel (30 g), using chloroform as eluent, to give the starting **8b** (144 mg) and a p-quinone **9b** (126 mg: 13.7%). The p-quinone **9b** was recrystallized from acetone-hexane, mp 225—226.5 °C, $[\alpha]_D$ +20.6° (c 1.41), IR 3615, 3540, 1670 sh, 1650, and 1637 cm^{-1}; ^{1}H NMR δ=1.01 (3H, s) and 1.26 (3H, s) ($-\overset{|}{C}(CH_3)_2$), 1.29 (3H, d, J=7 Hz, C_{15}-CH_3), 1.66 (3H, s, C_{10}-CH_3), 4.18 (1H, dd, J=6 and 9.5 Hz) and 4.70 (1H, t, J=9.5 Hz) (-OCH_2-), ca. 4.6 (1H, overlap, C_6-H). Found: C, 72.58; H, 7.79%. Calcd for $C_{20}H_{26}O_4$: C, 72.70; H, 7.93%.

(15*R*)-11,14-Diacetoxy-12,16-epoxy-8,11,13-abietatrien-6-one (10a) and Its (15*S*)-Epimer (10b). **a**): A mixture of **9a** (33.3 mg), acetic anhydride (1.0 ml), and zinc powder (50 mg) in pyridine (1.0 ml) was stirred at 0—5 °C for 1 h. After the addition of ether, the zinc powder was removed and the organic solution was washed successively with dilute hydrochloric acid, aqueous sodium hydrogencarbonate, and brine. The dried solution was evaporated in vacuo. The residue was oxidized with Jones reagent (2.5 mol dm^{-3}: 0.06 ml) in acetone (2.0 ml) with cooling in an ice-water bath for 3 min. After the addition of ether, the mixture was washed with water, dried, and evaporated in vacuo. The crude product was chromatographed on silica gel (5.0 g), using ether-benzene (3 : 97) as eluent, to give an oily **10a** (8.5 mg: 20%), IR 1763 and 1718 cm^{-1}, ^{1}H NMR (90 MHz) δ=1.01 (3H, s), 1.21 (3H, s), and 1.32 (3H, s) ($-\overset{|}{C}(CH_3)_2$ and C_{10}-CH_3), 1.23 (3H, d, J=7 Hz, C_{15}-CH_3), 2.29 (6H, s, C_{11}-$OCOCH_3$ and C_{14}-$OCOCH_3$), 2.62 (1H, s, C_5-H), 3.08 (1H, d, J=21 Hz) and 3.47 (1H, d, J=21 Hz) (-$COCH_2$-), 3.57 (1H, m, C_{15}-H), 4.13 (1H, dd, J=6.5 and 9 Hz) and 4.66 (1H, t, J=9 Hz) (-OCH_2-). Found: C, 69.25; H, 7.11%. Calcd for $C_{24}H_{30}O_6$: C, 69.54; H, 7.30%.

b): A mixture of **9b** (81.8 mg), acetic anhydride (1.0 ml), and zinc powder (30 mg) in pyridine (1.0 ml) was stirred at 0—5 °C for 1 h. After the work-up as described in **a**), the crude product was oxidized with Jones reagent (2.5 mol dm^{-3}: 0.15 ml) in acetone (1.0 ml) with cooling in an ice-water bath for 3 min. After the addition of ether, the mixture was washed with water, dried, and evaporated in vacuo. The residue was chromatographed on silica gel (10 g), using ether-benzene (3 : 97) as eluent, to give an oily **10b** (29.4 mg: 28.7%), $[\alpha]_D$ +48.2° (c 1.23), IR 1761 and 1718 cm^{-1}, ^{1}H NMR (90 MHz) δ=1.00 (3H, s), 1.21 (3H, s), and 1.31 (3H, s) ($-\overset{|}{C}(CH_3)_2$ and C_{10}-CH_3), 1.23 (3H, d, J=7 Hz, C_{15}-CH_3), 2.28 (6H, s, C_{11}-$OCOCH_3$ and C_{14}-$OCOCH_3$), 2.61 (1H, s, C_5-H), 3.15 (1H, d, J=21 Hz) and 3.42 (1H, d, J=21 Hz) (-$COCH_2$-), 3.57 (1H, m, C_{15}-H), 4.09 (1H, dd, J=6.5 and 9 Hz) and 4.69 (1H, t, J=9 Hz) (-OCH_2-). Found: C, 69.81; H, 7.59%. Calcd for $C_{24}H_{30}O_6$: C, 69.54; H, 7.30%.

(15*R*)-12,16-Epoxy-6,11,14-trihydroxy-5,8,11,13-abietate-

traen-7-one (Lycoxanthol) (1a) and Its (15*S*)-Epimer (1b). **a**): A stirred solution of **10a** (8.5 mg) in acetone (1.0 ml) was oxidized with Jones reagent (1 mol dm^{-3}: 0.1 ml) at room temperature for 2 h. The mixture was diluted with ether, washed with water, and evaporated in vacuo. The residue was dissolved in ethanol (1.0 ml) containing dilute hydrochloric acid (15%: 0.1 ml). The solution was refluxed for 5 h, cooled, and then diluted with ether. The ether solution was washed with water, dried, and evaporated in vacuo. The crude product was chromatographed on silica gel (Mallinckrodt CC-4, 7 g), using hexane-chloroform (1 : 2) as eluent, to give **1a** (2.2 mg: 31%) which was recrystallized from acetone-hexane, mp 250—251 °C, IR (KBr) 3485, 1640, and 1615 cm^{-1}; ^{1}H NMR (90 MHz) δ=1.40 (3H, d, *J*=7 Hz, C_{15}-CH_3), 1.44 (6H, s, -$\overset{|}{C}$(CH_3)$_2$), 1.65 (3H, s, C_{10}-CH_3), 3.80 (1H, m, C_{15}-H), 4.28 (1H, dd, *J*=9 and 6 Hz) and 4.81 (1H, t, *J*=9 Hz) (-OCH_2-), 12.55 (1H, s, C_{14}-OH); MS *m/z* 344 (M^+). The synthetic **1a** was identical with natural lycoxanthol (mp 249 °C).

b): A stirred solution of **10b** (29.4 mg) in acetone (2.0 ml) was oxidized with Jones reagent (2.5 mol dm^{-3}: 0.14 ml) at room temperature for 2 h. The crude product was hydrolyzed with dilute hydrochloric acid (15%: 0.1 ml) in refluxing ethanol (1.0 ml) for 5 h. After the work-up as described in **a**), the crude product was chromatographed on silica gel (Mallinckrodt CC-4, 7 g), using hexane-chloroform (1 : 2) as eluent, to give **1b** (9.8 mg: 40%). This was recrystallized from acetone-hexane, mp 219—220 °C, IR (KBr) 3395, 1637, and 1611 cm^{-1}; ^{1}H NMR (90 MHz) δ=1.42 (3H, d, *J*=7 Hz, C_{15}-CH_3), 1.44 (6H, s, -$\overset{|}{C}$(CH_3)$_2$), 1.66 (3H, s, C_{10}-CH_3), 3.75 (1H, m, C_{15}-H), 4.28 (1H, dd, *J*=9 and 6 Hz) and 4.80 (1H, t, *J*=9 Hz) (-OCH_2-), 12.55 (1H, s, C_{14}-OH); MS *m/z* 344 (M^+).

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4) Yields are based on the starting material consumed.