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The Synthesis of (15*R*)-Coleon C and (15*S*)-Coleon C

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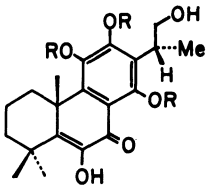
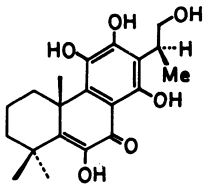
(15*R*)-11,16-Dihydroxy-12-methoxymethoxy-8,11,13-abietatrien-7-one and its (15*S*)-epimer prepared from a C-15 epimeric mixture of 12-methoxy-8,11,13-abietatrien-16-ol, were transformed into (15*R*)-6,11,12,14,16-pentahydroxy-5,8,11,13-abietatetraen-7-one and its (15*S*)-epimer; these were identical with natural (15*R*)-coleon C and (15*S*)-coleon C, respectively.

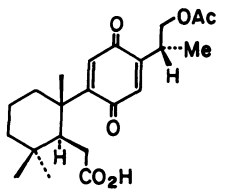
Coleon C was first isolated as a mixture of the C-15 epimers from the leaves of *Coleus aquaticus* Gürcke (Labiatae) by Eugster et al.;[1] they[2] later separated the mixture into (15*R*)-coleon C (**1a**) and (15*S*)-coleon C (**1b**). Recently, Burnell et al.[3] reported the synthesis of (15*R*)-coleon C tri-*O*-methyl ether (**2a**) via a (15*R*)-quinone intermediate (**3a**) which was prepared from 12,16-epoxy-8,11,13,15-abietatetraene (**4**) by the following series of reactions. Stereoselective catalytic hydrogenation of **4** gave a mixture of the C-15 epimeric 12,16-epoxy-8,11,13-abietatrienes (**5**) which was oxidized with chromium trioxide in acetic acid to give the epimeric 7-oxo compounds **6**. Further oxidation of **6** with hydrogen peroxide in acetic anhydride containing concentrated sulfuric acid produced two quinones, **3a** and its C-15 epimer **3b**, in a ratio of 5:2. Their stereochemical assignments of C-15 in **3a** and **3b** were based on the stereochemistries of C-15 in the catalytic hydrogenation products **5**, whose stereochemistries were assigned to be 15R for the major product and 15S for the minor product (from examinations of molecular models). However, it seemed to be necessary to confirm the stereochemistries of the hydrogenation products **5** by unambiguous methods. Very recently,[4] we also carried out the catalytic hydrogenation of **4** and assigned the stereochemistry of C-15 in the major product to have a S configuration in contrast to the assignment of Burnell et al. As an extension of our previous work,[4] we here describe the successful syntheses of (15*R*)-coleon C (**1a**) and (15*S*)-coleon C (**1b**) starting from a C-15 epimeric mixture of 12-methoxy-8,11,13-abietatrien-16-ol (**7**)[5] which was previously prepared from (+)-dehydroabietic acid.



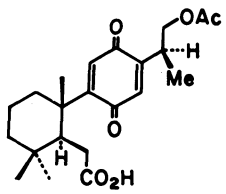
1a R=H
2a R=Me



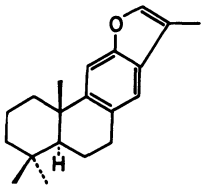
1b



3a



3b



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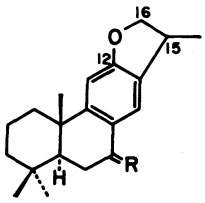
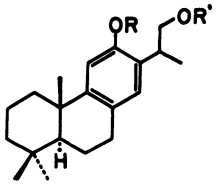


5 R=H$_2$
6 R=O

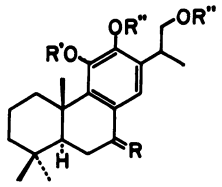
Mixture **7** was demethylated with anhydrous aluminium chloride and ethanethiol in dichloromethane to give a mixture of the corresponding diols **8** (90.3%). To introduce an oxygen function at the C-11 position, mixture **8** was submitted to a series of reactions: oxidation with benzoyl peroxide in refluxing chloroform, reduction with lithium aluminium hydride in ether, and acetylation with acetic anhydride in pyridine. Purification of the crude product by column chromatography on silica gel afforded a mixture of the C-15 epimeric triacetates **9** (50.6%) along with a mixture of the C-15 epimeric diacetates **10** (24.8%) which gave back the starting **8** (95.1%) by reduction with lithium aluminium hydride. Oxidation of **9** with chromium trioxide in acetic acid yielded a mixture of the 7-oxo compounds **11a** and **11b** (61.4%). This mixture was then hydrolyzed with dilute hydrochloric acid in refluxing methanol and the crude product was immediately methoxymethylated with a mixture of chloromethyl methyl ether, anhydrous potassium carbonate, and dicyclohexano-18-crown-6 in tetrahydrofuran–dichloromethane (1:1) at room temperature to give 12-methoxymethyl ethers **12a** and **12b** (73.6%) and 12,16-bis(methoxymethyl) ethers **13** (14.3%). The C-15 epimeric mixture of 12-methoxymethyl ether was carefully separated by repeated column chromatography on silica gel and recrystalliza-

tion to afford the pure crystalline 11,16-dihydroxy-12-methoxymethoxy-8,11,13-abietatrien-7-one (**12a**), mp 135—136 °C, and its C-15 epimer **12b**, mp 140—142 °C. In order to assign the absolute configurations of C-15 in these epimers, the compound **12a** was hydrolyzed with dilute hydrochloric acid in refluxing tetrahydrofuran and the resulting triol was acetylated with acetic anhydride in pyridine to give a triacetate (88.5%) which was identical with authentic (15*R*)-11,12,16-triacetoxy-8,11,13-abietatrien-7-one (**11a**).[5] On the other hand, the authentic (15*S*)-triacetate **11b**[5] was hydrolyzed with dilute hydrochloric acid in refluxing methanol and then partially methoxymethylated as described above. Purification of the crude product yielded (15*S*)-11,16-dihydroxy-12-methoxymethoxy-8,11,13-abietatrien-7-one (70.7%) which was identical with **12b**. Thus, the absolute configurations of C-15 in **12a** and **12b** were assigned to be R and S respectively.

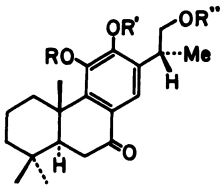
Subsequently, conversion of **12a** into (15*R*)-coleon C (**1a**) was carried out as follows. Hydrolysis of **12a** with dilute hydrochloric acid followed by methylation with diazomethane afforded 11,16-dihydroxy-12-methoxy-8,11,13-abietatrien-7-one (**14a**: 64.4%) together with small amounts of 11-hydroxy-12,16-methylenedioxy-8,11,13-abietatrien-7-one (**15a**: 19.8%) and 11-hydroxy-12,16-dimethoxy-8,11,13-abietatrien-7-one (**16a**: 13.9%). For the protection of the hydroxyl groups, **14a** was acetylated with acetic anhydride in pyridine to give a diacetate **17a** (93.9%). This was reduced with sodium borohydride in methanol and the resulting mixture of the epimeric 7-hydroxy compounds was immediately subjected to dehydration with *p*-toluenesulfonic acid in refluxing benzene to give 11,16-diacetoxy-12-methoxy-6,8,11,13-abietatetraene (**18a**: 86.8%). Epoxidation of **18a** with *m*-chloroperbenzoic acid in dichloromethane followed by treatment with *p*-toluenesulfonic acid in refluxing benzene afforded 11,16-diacetoxy-12-methoxy-8,11,13-abietatrien-6-one (**19a**: 79.6%). To introduce an oxygen function at the C-14 position, the 6-oxo compound **19a** was reduced with lithium aluminium hydride in ether and the resulting mixture of the epimeric 6-hydroxy compounds **20a** was immediately oxidized with *m*-chloroperbenzoic acid in methanol to give two *p*-quinones, **21a** (42.5%) and **22a** (6.6%). In the ^{1}H NMR spectrum of **21a**, the downfield shift of a signal (δ=1.69) due to the methyl group at C-10 relative to the corresponding signal (δ=1.36) for **22a** suggested a 1,3-diaxial-*cis*-relationship between the methyl group and the hydroxyl group at C-6. Thus, the structures of **21a** and **22a** were assigned to be 6β,16-dihydroxy-12-methoxy-8,12-abietadiene-11,14-dione and its 6α-hydroxy isomer respectively. Hydrolysis of **21a** with dilute hydrochloric acid in refluxing methanol afforded a trihydroxy quinone, which was partially acetylated with acetic anhydride in pyridine at 0—5 °C to give a 12,16-diacetoxy compound. This was further subjected to reductive acetylation with zinc powder and acetic anhydride in pyridine. The crude product

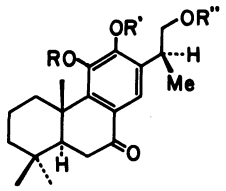


7 R=Me, R'=H
8 R=R'=H
10 R=R'=Ac

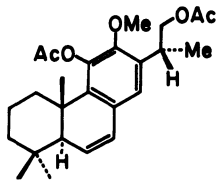


9 R=H$_2$, R'=R''=Ac
13 R=O, R'=H, R''=CH$_2$OMe

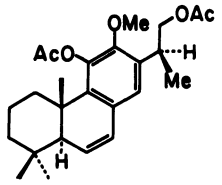




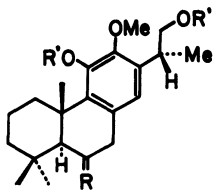
11a	R=R'=R''=Ac	11b
12a	R=R''=H, R'=CH$_2$OMe	12b
14a	R=R''=H, R'=Me	14b
15a	R=H, R'·R''=-CH$_2$-	15b
16a	R=H, R'=R''=Me	16b
17a	R=R''=Ac, R'=Me	17b

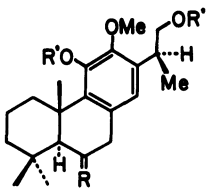


18a

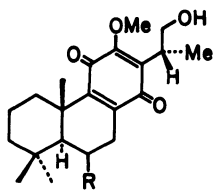


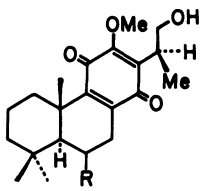
18b





19a	R=O, R'=Ac	19b
20a	R=H·OH, R'=H	20b

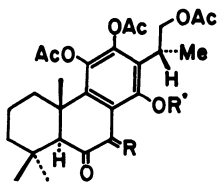




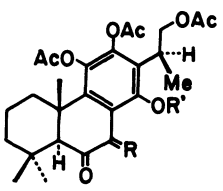
21a	R=β-OH	21b
22a	R=α-OH	22b

was then oxidized with Jones reagent at 0—5 °C to give 11,12,14,16-tetraacetoxy-8,11,13-abietatrien-6-one (**23a**: 21.9% from **21a**) and 11,12-diacetoxy-14,16-epoxy-8,11,13-abietatrien-6-one (**24a**: 23.5% from **21a**). The ^{1}H NMR spectrum of **23a** showed singlet (3H) signals at δ=2.00, 2.27, 2.29, and 2.32 due to four acetoxyl groups, while that of **24a** showed the corresponding signals at δ 2.25 and 2.27 ppm due to two acetoxyl groups and signals at δ=1.23 (3H, doublet), ca. 3.6 (1H, multiplet), 4.10 (1H, double doublet), and 4.69 (1H, triplet) due to a dihydrofuran moiety. The structure of **24a** was further supported from a similarity to its (15*S*)-epimer **24b** which is described later. To introduce a final oxygen function at the C-7 position, the tetraacetate **23a** was oxidized with Jones reagent at room temperature to afford 11,12,16-triacetoxy-14-hydroxy-8,11,13-abietatriene-6,7-dione [(15*R*)-coleon D triacetate] (**25a**: 27.4%). The presence of a hydroxyl group at C-14 in **25a** was supported by its ^{1}H NMR spectrum which showed a singlet signal due to a hydrogen-bonded hydroxyl group at δ 13.33. Compound **25a** was then hydrolyzed with dilute hydrochloric acid in refluxing methanol to give the desired 6,11,12,14,16-pentahydroxy-5,8,11,13-abietatetraen-7-one (**1a**: 98.9%) which was identical with natural (15*R*)-coleon C.

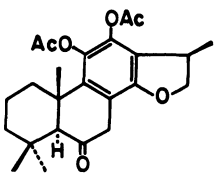
Similar conversion of (15*S*)-12-methoxymethyl ether **12b** into (15*S*)-coleon C (**1b**) was also carried out as follows. Hydrolysis of **12b** with dilute hydrochloric acid followed by methylation with diazomethane afforded 11,16-dihydroxy-12-methoxy-8,11,13-abietatrien-7-one (**14b**: 73.7%) along with small amounts of 12,16-methylenedioxy (**15b**: 13.9%) and 12,16-dimethoxy (**16b**: 12.1%) compounds. The 12-methoxy compound **14b** was acetylated and the resulting diacetate **17b** (90.2%) was transformed into 11,16-diacetoxy-12-methoxy-6,8,11,13-abietatetraene (**18b**: 83.0%) by sodium borohydride reduction and acid-catalyzed dehydration. Oxidation of **18b** with *m*-chloroperbenzoic acid followed by treatment with *p*-toluenesulfonic acid led to the corresponding 6-oxo compound **19b** (79.4%). This was converted into 6β,16-dihydroxy-12-methoxy-8,12-abietadiene-11,14-dione (**21b**: 38.7%) and its 6α-hydroxy isomer **22b** (9.1%) by reduction with lithium aluminium hydride and subsequent oxidation of the epimeric 6-hydroxy compounds **20b** with *m*-chloroperbenzoic acid. The *p*-quinone **21b** was then converted into tetraacetoxy ketone **23b** (66.1%) and diacetoxy ketone **24b** (31.8%) by a series of reactions; hydrolysis with dilute hydrochloric acid in methanol, acetylation with acetic anhydride in pyridine, reductive acetylation with zinc powder and acetic anhydride in pyridine, and oxidation with Jones reagent at 0—5 °C. The ^{1}H NMR spectrum of **24b** showed signals at δ 2.27 (6H, singlet) due to two acetoxyl groups and at δ 1.23 (3H, doublet), ca. 3.6 (1H, multiplet), 4.09 (1H, double doublet), and 4.69 (1H, triplet) due to a dihydrofuran moiety. For a structure determination of **24b**, the following conversion was carried out. Oxidation of the C-7 position in **24b** with Jones reagent afforded a mixture of the 6,7-dioxo compound **28b** and the diosphenol derivative **27b** which was hydrolyzed with dilute hydrochloric acid to give a phenolic compound **29b**. Since the ^{1}H NMR spectrum of **29b** showed no signal in the low field (δ=10—15) due to a hydrogen-bonded hydroxyl group at the C-14 position, the phenolic hydroxyl groups must be located at the C-11 and C-12 positions. Thus, the structure of **24b** was assigned to be 11,12-diacetoxy-14,16-epoxy-8,11,13-abietatrien-6-one. Further oxidation of **23b** with Jones reagent at room temperature produced 11,12,16-triacetoxy-14-hydroxy-8,11,13-abietatriene-6,7-dione [(15*S*)-coleon D triacetate] (**25b**: 54.4%). This was hydrolyzed with dilute hydrochloric acid in



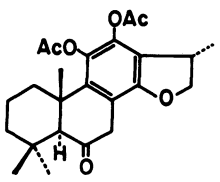
23a R=H$_2$, R'=Ac
25a R=O, R'=H



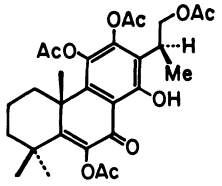
23b
25b



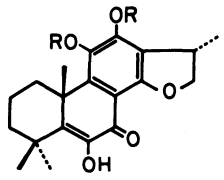
24a



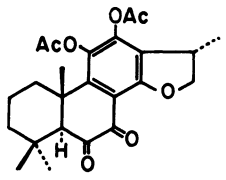
24b



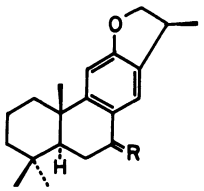
26b



27b R=Ac
29b R=H



28b



5b R=H$_2$
6b R=O

refluxing methanol to give the desired 6,11,12,14,16-pentahydroxy-5,8,11,13-abietatetraen-7-one (**1b**: 99.7%) which gave the corresponding 6,11,12,16-tetraacetoxy compound **26b** with acetic anhydride in pyridine. The synthetic **1b** was also identical with natural (15*S*)-coleon C.

Finally, in order to confirm the absolute configuration of C-15 in the reported coleon C tri-*O*-methyl ether,[3] (15*S*)-12,16-epoxy-8,11,13-abietatriene[4] (**5b**) prepared by unambiguous methods in our laboratory was converted into the (15*S*)-*p*-quinone **3b**, mp 148—150 °C, via (15*S*)-12,16-epoxy-8,11,13-abietatrien-7-one (**6b**) by the method of Burnell et al.[3] As we would expect, the physical and spectral data of the synthetic **3b** are in good agreement with those of the reported (15*R*)-*p*-quinone (mp 143—145 °C),[3] but different from those of the reported (15*S*)-*p*-quinone (mp 119—120 °C).[3] Therefore, the reported 15R configuration for coleon C tri-*O*-methyl ether and all other compounds derived from the major *p*-quinone in the articles of Burnell et al.[3] must be corrected to the reverse configuration (15*S*).

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).

8,11,13-Abietatriene-12,16-diol (8). Anhydrous aluminium chloride (8.407 g) was added to a stirred solution of 12-methoxy-8,11,13-abietatrien-16-ol (**7**)[5] (6.651 g) and ethanethiol (9.4 ml) in dichloromethane (67 ml) at 4—10 °C with cooling in an ice-water bath over a 12-min period. After stirring at this temperature for 10 min and at room temperature 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 residue was chromatographed on silica gel (60 g), using ether–benzene (4:96) as eluent, to give a mixture of the C-15 epimeric diols **8** (5.739 g: 90.3%).

11,12,16-Triacetoxy-8,11,13-abietatriene (9). A solution of **8** (12.062 g) and benzoyl peroxide (15.078 g) in chloroform (240 ml) was refluxed for 5 h, cooled, and diluted with ether (250 ml). After the addition of acetic acid (60 ml) and aqueous potassium iodide (30%: 200 ml), the mixture was stirred at room temperature for 2 h and then washed successively with water, aqueous sodium thiosulfate, aqueous sodium hydrogencarbonate, and brine. The dried solution was evaporated in vacuo to give the crude product, which was used, without purification, in the next reaction.

A solution of the above crude product in dry ether (80 ml) was added dropwise to a stirred suspension of lithium aluminium hydride (2.876 g) in dry ether (100 ml) with cooling in an ice-water bath over a 20-min period. The mixture was refluxed for 80 min, cooled; the excess lithium aluminium hydride was decomposed with ethyl acetate (20 ml). 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. The residue was acetylated with acetic anhydride (15 ml) in pyridine (15 ml) at 75—80 °C for 2 h. After the usual work-up, the crude product was chromatographed on silica gel (200 g), using ether–benzene (1:99) as eluent, to give 12,16-diacetoxy-8,11,13-abietatriene (**10**) (3.824 g: 24.8%). Further elution with ether–benzene (1:9) gave **9** (8.964 g: 50.6%). The IR and ^{1}H NMR spectra of **9** and **10** were identical with those of the corresponding (15*R*)-isomers or (15*S*)-isomers.[5]

A solution of **10** (3.782 g) in dry ether (25 ml) was added dropwise to a stirred suspension of lithium aluminium hydride (483 mg) in dry ether (25 ml) with cooling in an ice-water bath over a 10-min period. The mixture was refluxed for 1 h, poured into ice-dilute hydrochloric acid, and extracted with ether. The ether extract was washed with brine, dried, and evaporated in vacuo to give **8** (2.815 g: 95.1%).

11,12,16-Triacetoxy-8,11,13-abietatrien-7-one (11a,b). Chromium trioxide (4.177 g) was added to a stirred solution of **9** (9.771 g) in acetic acid (80 ml) with cooling in a water bath over a period of 1 h. The mixture was stirred at room temperature for 22 h, diluted with water, and extracted with ether. The ether extract was washed successively with water, aqueous sodium hydrogencarbonate, and brine. The dried solution was evaporated in vacuo. The residue was chromatographed on silica gel (250 g), using ether–benzene (4:96) as eluent, to give the recovered **9** (0.504 g: 5.2%) and a mixture of **11a** and **11b** (6.183 g: 61.4%).

11,16-Dihydroxy-12-methoxymethoxy-8,11,13-abietatrien-7-one (12a,b) and 11-Hydroxy-12,16-dimethoxymethoxy-8,11,13-abietatrien-7-one (13). A mixture of the triacetate (**11a,b**: 8.374 g) and dilute hydrochloric acid (15%: 15 ml) in methanol (80 ml) was refluxed for 2 h. After removal of the methanol in vacuo, the residue was extracted with ether. The ether extract was washed with water, dried, and evaporated in vacuo to give the crude triol (5.603 g).

A mixture of the crude triol (5.603 g), anhydrous potassium carbonate (3.028 g), and dicyclohexano-18-crown-6 (0.282 g) in tetrahydrofuran–dichloromethane (1:1, 100 ml) was stirred at room temperature for 30 min. After the addition of chloromethyl methyl ether (1.65 ml), the mixture was stirred at room temperature for 20 h and then diluted with ether. The ether solution was washed with brine, dried, and evaporated in vacuo. The residue was chromatographed on silica gel (250 g), using ether–benzene (1:9) as eluent, to give **13** (1.095 g: 14.3%) and a mixture of **12a** and **12b** (5.060 g: 73.6%). ^{1}H NMR of **13**: δ=0.94 (3H, s) and 0.97 (3H, s) (-C(CH$_3$)$_2$), 1.19 (d, J=7 Hz) and 1.23 (d, J=7 Hz) (3H, C$_{15}$-CH$_3$), 1.40 (3H, s, C$_{10}$-CH$_3$), 3.26 (3H, s, C$_{16}$-OCH$_2$OCH$_3$), 3.62 (3H, s, C$_{12}$-OCH$_2$OCH$_3$), 4.56 (2H, s, C$_{16}$-OCH$_2$OCH$_3$), 5.03 (2H, s, C$_{12}$-OCH$_2$OCH$_3$), 7.56 (1H, s, C$_{14}$-H).

The mixture (**12a,b**) was separated into the pure **12a**, mp 135—136 °C (from acetone–hexane), $[\alpha]_D$ +44.1° (c 3.93), IR: 3620, 3480, and 1678 cm^{-1}, and **12b**, mp 140—142 °C (from acetone–hexane), $[\alpha]_D$ +5.7° (c 21.98), IR: 3620, 3480, and 1678 cm^{-1}, by repeated column chromatography on silica

gel and recrystallization. ^{1}H NMR of **12a**: δ=0.94 (3H, s) and 0.98 (3H, s) (-C(CH$_3$)$_2$), 1.22 (3H, d, J=6.5 Hz, C$_{15}$-CH$_3$), 1.42 (3H, s, C$_{10}$-CH$_3$), 3.62 (3H, s, -OCH$_3$), 5.02 (2H, s, -OCH$_2$O-), 7.28 (1H, s, C$_{11}$-OH), 7.52 (1H, s, C$_{14}$-H). ^{1}H NMR of **12b**: δ=0.97 (3H, s) and 0.99 (3H, s) (-C(CH$_3$)$_2$), 1.19 (3H, d, J=6.5 Hz, C$_{15}$-CH$_3$), 1.42 (3H, s, C$_{10}$-CH$_3$), 3.63 (3H, s, -OCH$_3$), 5.07 (2H, s, -OCH$_2$O-), 7.32 (1H, s, C$_{11}$-OH), 7.56 (1H, s, C$_{14}$-H). Anal. of **12a**; Found: C, 70.46; H, 8.66%. Calcd for $C_{22}H_{32}O_5$: C, 70.18; H, 8.57%. Anal. of **12b**; Found: C, 70.40; H, 8.82%. Calcd for $C_{22}H_{32}O_5$: C, 70.18; H, 8.57%.

Conversion of 12a into (15*R*)-11,12,16-Triacetoxy-8,11,13-abietatrien-7-one (11a). A mixture of **12a** (155.0 mg) and dilute hydrochloric acid (15%: 0.2 ml) in tetrahydrofuran (1.0 ml) was refluxed for 3 h. The mixture was cooled, diluted with ether, and then washed with brine. The dried solution was evaporated in vacuo to give (15*R*)-11,12,16-trihydroxy-8,11,13-abietatrien-7-one which was recrystallized from acetone-hexane, mp 250—252 °C. ^{1}H NMR (acetone-d_6) δ=0.95 (3H, s) and 0.99 (3H, s) (-C(CH$_3$)$_2$), 1.29 (3H, d, J=7 Hz, C$_{15}$-CH$_3$), 1.41 (3H, s, C$_{10}$-CH$_3$), 7.33 (1H, s, C$_{14}$-H).

The above trihydroxy ketone was acetylated with acetic anhydride (0.5 ml) in pyridine (0.5 ml) at 85—90 °C for 2 h. After the usual work-up, the crude product was chromatographed on silica gel (10 g), using ether-benzene (5:95) as eluent, to give **11a** (167.0 mg: 88.5%), $[\alpha]_D$ +65.0° (c 2.77). The IR and ^{1}H NMR spectra of **11a** were identical with those of authentic (15*R*)-11,12,16-triacetoxy-8,11,13-abietatrien-7-one.[5]

Conversion of (15*S*)-11,12,16-Triacetoxy-8,11,13-abietatrien-7-one (11b) into 12b. A mixture of **11b**[5] (3.251 g) and dilute hydrochloric acid (15%: 5.0 ml) in methanol (30 ml) was refluxed for 2 h. After removal of the methanol in vacuo, the residue was extracted with ether. The ether extract was washed with brine, dried, and evaporated in vacuo to give (15*S*)-11,12,16-trihydroxy-8,11,13-abietatrien-7-one which was recrystallized from acetone-hexane, mp 228—230 °C, ^{1}H NMR (acetone-d_6) δ=0.97 (3H, s) and 1.01 (3H, s) (-C(CH$_3$)$_2$), 1.30 (3H, d, J=7 Hz, C$_{15}$-CH$_3$), 1.44 (3H, s, C$_{10}$-CH$_3$), 7.42 (1H, s, C$_{14}$-H).

A mixture of the above trihydroxy ketone (2.500 g), anhydrous potassium carbonate (1.274 g), and dicyclohexano-18-crown-6 (187 mg) in tetrahydrofuran-dichloromethane (1:1, 40 ml) was stirred at room temperature for 30 min. After the addition of chloromethyl methyl ether (0.69 ml), the mixture was stirred at room temperature for 18 h and then diluted with ether. The ether solution was washed with brine, dried, and evaporated in vacuo. The residue was chromatographed on silica gel (100 g), using ether-benzene (2:8) as eluent, to give (15*S*)-11,16-dihydroxy-12-methoxymethoxy-8,11,13-abietatrien-7-one (1.886 g: 70.7%), mp 140—142 °C (from acetone-hexane), whose IR and ^{1}H NMR spectra were identical with those of **12b**.

Hydrolysis and Methylation of 12a. A mixture of **12a** (1.580 g) and dilute hydrochloric acid (15%: 1.0 ml) in tetrahydrofuran (10 ml) was refluxed for 1.5 h. After removal of the tetrahydrofuran in vacuo, the reidue was extracted with ether. The ether extract was washed with brine, dried, and evaporated in vacuo to give the crude trihydroxy ketone.

A suspension of the above trihydroxy ketone in acetone-ether (1:4, 25 ml) was methylated with diazomethane in ether at room temperature for 3 h. After the usual work-up, the crude product was recrystallized from acetone-hexane to give (15*R*)-11,16-dihydroxy-12-methoxy-8,11,13-abietatrien-7-one (**14a**) (650 mg: 44.7%), mp 199—200.5 °C, $[\alpha]_D$ +41.2° (c 2.50), IR: 3490 and 1675 cm^{-1}; ^{1}H NMR δ=0.95 (3H, s) and 0.99 (3H, s) (-C(CH$_3$)$_2$), 1.26 (3H, d, J=7 Hz, C$_{15}$-CH$_3$), 1.42 (3H, s, C$_{10}$-CH$_3$), 3.73 (2H, bd, J=7 Hz, -CH$_2$OH), 3.84 (3H, s, -OCH$_3$), 6.29 (1H, s, C$_{11}$-OH), 7.58 (1H, s, C$_{14}$-H). Found: C, 72.71; H, 8.64%. Calcd for $C_{21}H_{30}O_4$: C, 72.80; H, 8.73%. The mother liquor of recrystallization was evaporated in vacuo and the residue was chromatographed on silica gel (50 g), using ether-benzene (1:9) as eluent, to give (15*R*)-11-hydroxy-12,16-methylenedioxy-8,11,13-abietatrien-7-one (**15a**) (286 mg: 19.8%) which was recrystallized from acetone-hexane, mp 182.5—183 °C, $[\alpha]_D$ +94.8° (c 1.54), IR: 3510 and 1675 cm^{-1}; ^{1}H NMR δ=0.95 (3H, s) and 0.99 (3H, s) (-C(CH$_3$)$_2$), 1.32 (3H, d, J=7 Hz, C$_{15}$-CH$_3$), 1.40 (3H, s, C$_{10}$-CH$_3$), 4.77 (1H, d, J=7 Hz) and 5.37 (1H, d, J=7 Hz) (-OCH$_2$O-), 6.24 (1H, s, C$_{11}$-OH), 7.49 (1H, s, C$_{14}$-H). MS (m/z): 344 (M$^+$). Found: C, 73.32; H, 8.28%. Calcd for $C_{21}H_{28}O_4$: C, 73.22; H, 8.19%.

Subsequent elution gave (15*R*)-11-hydroxy-12,16-dimethoxy-8,11,13-abietatrien-7-one (**16a**) (210 mg: 13.9%) which was recrystallized from hexane, mp 181—182.5 °C, $[\alpha]_D$ +20.0° (c 2.00), IR: 3505 and 1676 cm^{-1}, ^{1}H NMR δ=0.95 (3H, s) and 0.99 (3H, s) (-C(CH$_3$)$_2$), 1.23 (3H, d, J=6.5 Hz, C$_{15}$-CH$_3$), 1.41 (3H, s, C$_{10}$-CH$_3$), 3.31 (3H, s, C$_{16}$-OCH$_3$), 3.82 (3H, s, C$_{12}$-OCH$_3$), 6.11 (1H, s, C$_{11}$-OH), 7.59 (1H, s, C$_{14}$-H). Found: C, 73.17; H, 9.24%. Calcd for $C_{22}H_{32}O_4$: C, 73.30; H, 8.95%.

Further elution with ether-benzene (1:4) gave an additional **14a** (287 mg: 19.7%).

Hydrolysis and Methylation of 12b. The 12-methoxymethyl ether **12b** (690 mg) was hydrolyzed with dilute hydrochloric acid (15%: 0.5 ml) in refluxing tetrahydrofuran (5.0 ml) for 1.5 h. The crude trihydroxy ketone was then methylated with diazomethane in ether at room temperature for 4 h to give the following three compound **14b**, **15b**, and **16b**.

(15*S*)-11,16-Dihydroxy-12-methoxy-8,11,13-abietatrien-7-one (**14b**) (468 mg: 73.7%), mp 240—241 °C (from acetone-hexane), $[\alpha]_D$ −18.8° (c 0.59), ^{1}H NMR δ=0.94 (3H, s) and 0.98 (3H, s) (-C(CH$_3$)$_2$), 1.22 (3H, d, J=7 Hz, C$_{15}$-CH$_3$), 1.40 (3H, s, C$_{10}$-CH$_3$), 3.70 (2H, bd, J=7 Hz, -CH$_2$OH), 3.82 (3H, s, -OCH$_3$), 6.09 (1H, s, C$_{11}$-OH), 7.59 (1H, s, C$_{14}$-H). Found: C, 72.58; H, 8.67%. Calcd for $C_{21}H_{30}O_4$: C, 72.80; H, 8.73%.

(15*S*)-11-Hydroxy-12,16-methylenedioxy-8,11,13-abietatrien-7-one (**15b**) (88 mg: 13.9%), mp 210—211 °C (from acetone-hexane), $[\alpha]_D$ −41.0° (c 1.88), ^{1}H NMR: δ=0.97 (3H, s) and 1.00 (3H, s) (-C(CH$_3$)$_2$), 1.35 (3H, d, J=7 Hz, C$_{15}$-CH$_3$), 1.42 (3H, s, C$_{10}$-CH$_3$), 4.80 (1H, d, J=7 Hz) and 5.38 (1H, d, J=7 Hz) (-OCH$_2$O-), 6.35 (1H, s, C$_{11}$-OH), 7.53 (1H, s, C$_{14}$-H). Found: C, 73.24; H, 7.91%. Calcd for $C_{21}H_{28}O_4$: C, 73.22; H, 8.19%.

(15*S*)-11-Hydroxy-12,16-dimethoxy-8,11,13-abietatrien-7-one (**16b**) (80 mg: 12.1%), mp 169.5—171 °C (from hexane), $[\alpha]_D$ +9.2° (c 1.20), ^{1}H NMR δ=0.97 (3H, s) and 1.00 (3H, s)

(-C(CH$_3$)$_2$), 1.24 (3H, d, J=6.5 Hz, C$_{15}$-CH$_3$), 1.42 (3H, s, C$_{10}$-CH$_3$), 3.35 (3H, s, C$_{16}$-OCH$_3$), 3.84 (3H, s, C$_{12}$-OCH$_3$), 6.18 (1H, s, C$_{11}$-OH), 7.60 (1H, s, C$_{14}$-H). Found: C, 73.29; H, 8.93%. Calcd for $C_{22}H_{32}O_4$: C, 73.30; H, 8.95%.

(15*R*)-11,16-Diacetoxy-12-methoxy-8,11,13-abietatrien-7-one (17a) and Its (15*S*)-Epimer (17b). *a*): A mixture of **14a** (1.441 g) and acetic anhydride (3.0 ml) in pyridine (4.0 ml) was heated at 75—80 °C for 2 h. After the usual work-up, the crude product was chromatographed on silica gel (30 g), using ether-benzene (1:9) as eluent, to give **17a** (1.681 g: 93.9%), $[\alpha]_D$ +51.9° (*c* 10.01), IR: 1767, 1733, and 1680 cm^{-1}; ^{1}H NMR δ=0.98 (3H, s) and 1.00 (3H, s) (-C(CH$_3$)$_2$), 1.31 (3H, d, J=7 Hz, C$_{15}$-CH$_3$), 1.37 (3H, s, C$_{10}$-CH$_3$), 2.03 (3H, s, C$_{16}$-OCOCH$_3$), 2.38 (3H, s, C$_{11}$-OCOCH$_3$), 3.48 (1H, m, C$_{15}$-H), 3.79 (3H, s, C$_{12}$-OCH$_3$), 4.13 (2H, bd, J=7 Hz, -CH$_2$OAc), 7.98 (1H, s, C$_{14}$-H). Found: C, 69.86; H, 7.85%. Calcd for $C_{25}H_{34}O_6$: C, 69.74; H, 7.96%.

b): A mixture of **14b** (410.0 mg) and acetic anhydride (2.0 ml) in pyridine (3.0 ml) was heated at 75—80 °C for 2 h to give **17b** (459.6 mg: 90.2%), $[\alpha]_D$ +13.0° (*c* 2.77), IR: 1767, 1733, and 1680 cm^{-1}; ^{1}H NMR δ=0.98 (3H, s) and 1.00 (3H, s) (-C(CH$_3$)$_2$), 1.28 (3H, d, J=7 Hz, C$_{15}$-CH$_3$), 1.37 (3H, s, C$_{10}$-CH$_3$), 2.03 (3H, s, C$_{16}$-OCOCH$_3$), 2.38 (3H, s, C$_{11}$-OCOCH$_3$), 3.46 (1H, m, C$_{15}$-H), 3.78 (3H, s, C$_{12}$-OCH$_3$), 4.16 (2H, bd, J=7 Hz, -CH$_2$OAc), 7.97 (1H, s, C$_{14}$-H). Found: C, 69.54; H, 8.21%. Calcd for $C_{25}H_{34}O_6$: C, 69.74; H, 7.96%.

(15*R*)-11,16-Diacetoxy-12-methoxy-6,8,11,13-abietatetraene (18a) and Its (15*S*)-Epimer (18b). *a*): A mixture of **17a** (915.5 mg) and sodium borohydride (40.2 mg) in methanol (5.0 ml) was stirred at 0—5 °C for 30 min and at room temperature for 1 h. The mixture was diluted with ether, acidified with dilute hydrochloric acid, and then extracted with ether. The ether extract was washed with brine, dried, and evaporated in vacuo. The residue was refluxed with *p*-toluenesulfonic acid (100 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 (40 g), using ether-benzene (5:95) as eluent, to give **18a** (765.2 mg: 86.8%). This was recrystallized from hexane, mp 79.5—81 °C, $[\alpha]_D$ −76.9° (*c* 4.85), IR: 1745sh and 1730 cm^{-1}; ^{1}H NMR δ=0.98 (3H, s) and 1.02 (3H, s) (-C(CH$_3$)$_2$), 1.12 (3H, s, C$_{10}$-CH$_3$), 1.26 (3H, d, J=7 Hz, C$_{15}$-CH$_3$), 2.01 (3H, s, C$_{16}$-OCOCH$_3$), 2.31 (3H, s, C$_{11}$-OCOCH$_3$), 3.71 (3H, s, C$_{12}$-OCH$_3$), 4.08 (2H, d, J=7 Hz, -CH$_2$OAc), 5.89 (1H, dd, J=9.5 and 3 Hz, C$_6$-H), 6.43 (1H, dd, J=9.5 and 3 Hz, C$_7$-H), 6.78 (1H, s, C$_{14}$-H). Found: C, 72.20; H, 8.30%. Calcd for $C_{25}H_{34}O_5$: C, 72.43; H, 8.27%.

b): The ketone **17b** (437.0 mg) was treated as described in *a*) to give **18b** (349.4 mg: 83.0%), $[\alpha]_D$ −74.0° (*c* 2.65), IR: 1745sh and 1730 cm^{-1}, ^{1}H NMR δ=0.98 (3H, s) and 1.02 (3H, s) (-C(CH$_3$)$_2$), 1.12 (3H, s, C$_{10}$-CH$_3$), 1.22 (3H, d, J=7 Hz, C$_{15}$-CH$_3$), 2.03 (3H, s, C$_{16}$-OCOCH$_3$), 2.32 (3H, s, C$_{11}$-OCOCH$_3$), 3.72 (3H, s, C$_{12}$-OCH$_3$), 4.15 (2H, d, J=7 Hz, -CH$_2$OAc), 5.92 (1H, dd, J=9.5 and 3 Hz, C$_6$-H), 6.45 (1H, dd, J=9.5 and 3 Hz, C$_7$-H), 6.78 (1H, s, C$_{14}$-H). Found: C, 72.51; H, 8.18%. Calcd for $C_{25}H_{34}O_5$: C, 72.43; H, 8.27%.

(15*R*)-11,16-Diacetoxy-12-methoxy-8,11,13-abietatrien-6-one (19a) and Its (15*S*)-Epimer (19b). *a*): A mixture of **18a** (1.335 g) and *m*-chloroperbenzoic acid (80%: 1.042 g) in dichloromethane (10 ml) was stirred at 0—5 °C for 30 min and at room temperature for 2.5 h. The mixture was diluted with ether (30 ml) 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 (100 mg) in dry benzene (10 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 (30 g), using ether-benzene (1:9) as eluent, to give an oily **19a** (1.104 g: 79.6%), $[\alpha]_D$ +92.1° (*c* 6.17), IR: 1767 and 1720 cm^{-1}, ^{1}H NMR δ=1.06 (3H, s), 1.23 (3H, s), and 1.33 (3H, s) (-C(CH$_3$)$_2$ and C$_{10}$-CH$_3$), 1.28 (3H, d, J=7 Hz, C$_{15}$-CH$_3$), 2.03 (3H, s, C$_{16}$-OCOCH$_3$), 2.36 (3H, s, C$_{11}$-OCOCH$_3$), 2.59 (1H, s, C$_5$-H), 3.72 (3H, s, C$_{12}$-OCH$_3$), 4.10 (2H, d, J=7 Hz, -CH$_2$OAc), 6.78 (1H, s, C$_{14}$-H). Found: C, 69.84; H, 7.91%. Calcd for $C_{25}H_{34}O_6$: C, 69.74; H, 7.96%.

b): The tetraene **18b** (1.019 g) was treated as described in *a*) to give an oily **19b** (840 mg: 79.4%), $[\alpha]_D$ +84.7° (*c* 2.36), IR: 1765 and 1720 cm^{-1}, ^{1}H NMR δ=1.06 (3H, s), 1.23 (3H, s), and 1.33 (3H, s) (-C(CH$_3$)$_2$ and C$_{10}$-CH$_3$), 1.23 (3H, d, J=7 Hz, C$_{15}$-CH$_3$), 2.03 (3H, s, C$_{16}$-OCOCH$_3$), 2.36 (3H, s, C$_{11}$-OCOCH$_3$), 2.58 (1H, s, C$_5$-H), 3.72 (3H, s, C$_{12}$-OCH$_3$), 4.14 (2H, d, J=7 Hz, -CH$_2$OAc), 6.79 (1H, s, C$_{14}$-H). Found: C, 69.59; H, 7.68%. Calcd for $C_{25}H_{34}O_6$: C, 69.74; H, 7.96%.

Conversion of 19a into (15*R*)-6β,16-Dihydroxy-12-methoxy-8,12-abietadiene-11,14-dione (21a) and Its 6α-Hydroxy Isomer (22a). A mixture of **19a** (1.074 g) and lithium aluminium hydride (142 mg) in dry ether (10 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 mixture of the C-6 epimeric triols **20a** (822 mg). This was recrystallized from acetone-hexane to give (15*R*)-12-methoxy-8,11,13-abietatriene-6β,11,16-triol, mp 201—203 °C, IR (KBr): 3515 and 3490—3350 cm^{-1}, ^{1}H NMR (acetone-d_6) δ=1.02 (3H, s) and 1.30 (3H, s) (-C(CH$_3$)$_2$), 1.20 (3H, d, J=7 Hz, C$_{15}$-CH$_3$), 1.72 (3H, s, C$_{10}$-CH$_3$), 3.69 (3H, s, C$_{12}$-OCH$_3$), 4.57 (1H, m, $W_{1/2}$=7 Hz, C$_6$-H), 6.35 (1H, s, C$_{14}$-H). Found: C, 72.47; H, 9.34%. Calcd for $C_{21}H_{32}O_4$: C, 72.38; H, 9.26%.

A mixture of **20a** (503 mg) and *m*-chloroperbenzoic acid (80%: 623 mg) in methanol (7.0 ml) was stirred at room temperature for 4 h and then diluted with ether (50 ml). 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 (30 g), using ether-chloroform (1:9) as eluent, to give **21a** (235 mg: 42.5%) which was recrystallized from acetone-hexane, mp 178—180 °C, $[\alpha]_D$ −73.8° (*c* 0.65). IR: 3600, 3450, 1658, and 1638 cm^{-1}; ^{1}H NMR δ=1.01 (3H, s) and 1.27 (3H, s) (-C(CH$_3$)$_2$), 1.18 (3H, d, J=7 Hz, C$_{15}$-CH$_3$), 1.69 (3H, s, C$_{10}$-CH$_3$), 3.72 (2H, bd, J=7 Hz, -CH$_2$OH), 3.91 (3H, s, C$_{12}$-OCH$_3$), 4.62 (1H, $W_{1/2}$=8 Hz, C$_6$-H). Found: C, 69.81; H, 8.37%. Calcd for $C_{21}H_{30}O_5$: C, 69.58; H, 8.34%. Further elution with ether-chloroform (1:4) gave **22a** as an

oil (37 mg: 6.6%), ^{1}H NMR δ=1.13 (3H, s) and 1.20 (3H, s) (-C(CH$_3$)$_2$), 1.16 (3H, d, J=7 Hz, C$_{15}$-CH$_3$), 1.36 (3H, s, C$_{10}$-CH$_3$), 3.87 (3H, s, C$_{12}$-OCH$_3$).

Conversion of 19b into (15*S*)-6β,16-Dihydroxy-12-methoxy-8,12-abietadiene-11,14-dione (21b) and Its 6α-Hydroxy Isomer (22b). A mixture of **19b** (725.0 mg) and lithium aluminium hydride (95.9 mg) in dry ether (8.0 ml) was refluxed for 1.5 h. The crude product **20b** (533.8 mg) was recrystallized from acetone-hexane to give (15*S*)-12-methoxy-8,11,13-abietatriene-6β,11,16-triol, mp 186—188 °C, IR (KBr): 3480 and 3370 cm^{-1}, ^{1}H NMR (acetone-d_6) δ=1.03 (3H, s) and 1.31 (3H, s) (-C(CH$_3$)$_2$), 1.19 (3H, d, J=7 Hz, C$_{15}$-CH$_3$), 1.73 (3H, s, C$_{10}$-CH$_3$), 3.71 (3H, s, C$_{12}$-OCH$_3$), 4.60 (1H, $W_{1/2}$=7 Hz, C$_6$-H), 6.38 (1H, s, C$_{14}$-H). Found: C, 72.25; H, 9.18%. Calcd for C$_{21}$H$_{32}$O$_4$: C, 72.38; H, 9.26%.

A mixture of **20b** (310.4 mg) and *m*-chloroperbenzoic acid (80%: 384.3 mg) in methanol (5.0 ml) was stirred at room temperature for 4 h. The crude product was chromatographed on silica gel (20 g), using ether-chloroform (1:4) as eluent, to give **21b** (137.3 mg: 38.7%) which was recrystallized from acetone-hexane, mp 183—185 °C, [α]$_D$ −63.6° (c 2.06), IR: 3615, 3450, 1660, 1642, and 1602 cm^{-1}; ^{1}H NMR δ=0.99 (3H, s) and 1.25 (3H, s) (-C(CH$_3$)$_2$), 1.14 (3H, d, J=7 Hz, C$_{15}$-CH$_3$), 1.67 (3H, s, C$_{10}$-CH$_3$), 3.72 (2H, bd, J=7 Hz, -CH$_2$OH), 3.91 (3H, s, C$_{12}$-OCH$_3$), 4.60 (1H, $W_{1/2}$=8 Hz, C$_6$-H). Found: C, 69.31; H, 8.48%. Calcd for C$_{21}$H$_{30}$O$_5$: C, 69.58; H, 8.34%. Further elution gave **22b** as an oil (32.3 mg: 9.1%), IR: 3600, 3450, 1660, and 1640 cm^{-1}; ^{1}H NMR δ=1.12 (3H, s) and 1.20 (3H, s) (-C(CH$_3$)$_2$), 1.15 (3H, d, J=7 Hz, C$_{15}$-CH$_3$), 1.36 (3H, s, C$_{10}$-CH$_3$), 3.88 (3H, s, C$_{12}$-OCH$_3$).

(15*R*)-11,12,14,16-Tetraacetoxy-8,11,13-abietatrien-6-one (23a) and (15*R*)-11,12-Diacetoxy-14,16-epoxy-8,11,13-abietatrien-6-one (24a). A mixture of **21a** (341.5 mg) and dilute hydrochloric acid (5%: 0.3 ml) in methanol (3.0 ml) was refluxd for 30 min and then diluted with ethyl acetate. The solution was washed with water, dried, and evaporated in vacuo to give a crude triol, ^{1}H NMR δ=1.01 (3H, s) and 1.27 (3H, s) (-C(CH$_3$)$_2$), 1.63 (3H, s, C$_{10}$-CH$_3$), 4.60 (1H, $W_{1/2}$=7 Hz, C$_6$-H).

The crude triol was acetylated with acetic anhydride (1.0 ml) in pyridine (3.0 ml) at 0—5 °C for 1 h. The mixture was diluted with ethyl acetate and washed successively with dilute hydrochloric acid, aqueous sodium hydrogencarbonate, and brine. The dried solution was evaporated in vacuo to give a crude diacetate, ^{1}H NMR δ=1.01 (3H, s) and 1.27 (3H, s) (-C(CH$_3$)$_2$), 1.67 (3H, s, C$_{10}$-CH$_3$), 1.99 (3H, s, C$_{16}$-OCOCH$_3$), 2.31 (3H, s, C$_{12}$-OCOCH$_3$), 4.21 (2H, d, J=7 Hz, -CH$_2$OAc), 4.62 (1H, $W_{1/2}$=7 Hz, C$_6$-H).

A mixture of the crude diacetate, acetic anhydride (1.0 ml), and zinc powder (90 mg) in pyridine (3.0 ml) was stirred at 0—5 °C for 1 h. After the addition of ether, 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}: 0.57 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 (12 g), using ether-benzene (1:99) as eluent, to give **24a** (91.9 mg: 23.5%), [α]$_D$ +53.2° (c 1.32), IR: 1770 and 1719 cm^{-1}, ^{1}H NMR (90 MHz) δ=1.01 (3H, s), 1.22 (3H, s), and 1.33 (3H, s) (-C(CH$_3$)$_2$ and C$_{10}$-CH$_3$), 1.23 (3H, d, J=7 Hz, C$_{15}$-CH$_3$), 2.25 (3H, s) and 2.27 (3H, s) (C$_{11}$-OCOCH$_3$ and C$_{12}$-OCOCH$_3$), 2.60 (1H, s, C$_5$-H), 3.18 (1H, d, J=21 Hz) and 3.57 (1H, d, J=21 Hz) (-COCH$_2$-), 4.10 (1H, dd, J=7 and 8 Hz) and 4.69 (1H, t, J=9 Hz) (-OCH$_2$-). Found: C, 69.67; H, 7.43%. Calcd for C$_{24}$H$_{30}$O$_6$: C, 69.54; H, 7.30%. Further elution with ether-benzene (1:9) gave **23a** (106.6 mg: 21.9%) which was recrystallized from methanol, mp 214.5—217.5 °C, [α]$_D$ +37.4° (c 1.23), IR: 1776 and 1725 cm^{-1}, ^{1}H NMR (90 MHz) δ=1.01 (3H, s), 1.19 (3H, s), and 1.31 (3H, s) (-C(CH$_3$)$_2$ and C$_{10}$-CH$_3$), 1.18 (3H, d, J=7 Hz, C$_{15}$-CH$_3$), 2.00 (3H, s, C$_{16}$-OCOCH$_3$), 2.27 (3H, s), 2.29 (3H, s), and 2.32 (3H, s) (C$_{11}$-OCOCH$_3$, C$_{12}$-OCOCH$_3$, and C$_{14}$-OCOCH$_3$), 2.62 (1H, s, C$_5$-H), 3.16 (1H, d, J=21 Hz) and 3.42 (1H, d, J=21 Hz) (-COCH$_2$-), 4.03 (1H, dd, J=8 and 9.5 Hz) and 4.30 (1H, dd, J=8 and 9.5 Hz) (-CH$_2$OAc). Found: C, 65.38; H, 7.29%. Calcd for C$_{28}$H$_{36}$O$_9$: C, 65.10; H, 7.03%.

(15*S*)-11,12,14,16-Tetraacetoxy-8,11,13-abietatrien-6-one (23b) and (15*S*)-11,12-Diacetoxy-14,16-epoxy-8,11,13-abietatrien-6-one (24b). The quinone **21b** (19.0 mg) was hydrolyzed with dilute hydrochloric acid (5%: 0.1 ml) in refluxing methanol (1.0 ml) for 30 min to give a crude triol (19.0 mg), ^{1}H NMR δ=1.01 (3H, s) and 1.25 (3H, s) (-C(CH$_3$)$_2$), 1.28 (3H, d, J=7 Hz, C$_{15}$-CH$_3$), 1.61 (3H, s, C$_{10}$-CH$_3$), 4.60 (1H, $W_{1/2}$=7 Hz, C$_6$-H).

The crude triol (19.0 mg) was acetylated with acetic anhydride (0.5 ml) in pyridine (0.5 ml) at 0—5 °C for 1 h to give a crude diacetate (20.0 mg), ^{1}H NMR δ=1.00 (3H, s) and 1.25 (3H, s) (-C(CH$_3$)$_2$), 1.64 (3H, s, C$_{10}$-CH$_3$), 1.97 (3H, s, C$_{16}$-OCOCH$_3$), 2.30 (3H, s, C$_{12}$-OCOCH$_3$), 4.20 (2H, d, J=7 Hz, -CH$_2$OAc), 4.62 (1H, $W_{1/2}$=7 Hz, C$_6$-H).

A mixture of the crude diacetate (20.0 mg), acetic anhydride (0.5 ml), and zinc powder (50 mg) in pyridine (0.5 ml) was stirred at 0—5 °C for 1 h. After the addition of ether, zinc powder was removed and the ether solution was washed successively with dilute hydrochloric acid, aqueous sodium hydrogencarbonate, and brine. The dried solution was evaporated in vacuo to give an oil (26.0 mg).

The above oil (26.0 mg) in acetone (1.0 ml) was oxidized with Jones reagent (2.5 mol dm^{-3}: 0.03 ml) at 0—5 °C for 3 min. After the addition of ether and water, the ether solution was washed with brine, dried, and evaporated in vacuo. The residue was chromatographed on silica gel (5 g), using ether-benzene (5:95) as eluent, to give **24b** (6.9 mg: 31.8%) which was recrystallized from acetone-hexane, mp 186.5—188.5 °C, [α]$_D$ +107.2° (c 2.92), IR: 1769 and 1720 cm^{-1}, ^{1}H NMR (90 MHz) δ=1.02 (3H, s), 1.20 (3H, s), and 1.32 (3H, s) (-C(CH$_3$)$_2$ and C$_{10}$-CH$_3$), 1.23 (3H, d, J=7 Hz, C$_{15}$-CH$_3$), 2.27 (6H, s, C$_{11}$-OCOCH$_3$ and C$_{12}$-OCOCH$_3$), 2.63 (1H, s, C$_5$-H), 3.18 (1H, d, J=21 Hz) and 3.57 (1H, d, J=21 Hz) (-COCH$_2$-), 4.09 (1H, dd, J=7 and 8 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%. Further elution with ether-benzene (1:9) gave **23b** as an oil (17.9 mg: 66.1%), [α]$_D$ +77.4° (c 0.84), IR: 1771 and 1721 cm^{-1}, ^{1}H NMR (90 MHz) δ=1.01 (3H, s), 1.20 (3H, s), and 1.32 (3H, s) (-C(CH$_3$)$_2$ and C$_{10}$-CH$_3$), 1.18 (3H, d, J=7 Hz,

C_{15}-CH_3), 2.00 (3H, s, C_{16}-$OCOCH_3$), 2.27 (3H, s), 2.29 (3H, s), and 2.33 (3H, s) (C_{11}-$OCOCH_3$, C_{12}-$OCOCH_3$, and C_{14}-$OCOCH_3$), 2.63 (1H, s, C_5-H), 3.16 (1H, d, J=21 Hz) and 3.42 (1H, d, J=21 Hz) (-$COCH_2$-), 4.03 (1H, dd, J=8 and 9.5 Hz) and 4.30 (1H, dd, J=8 and 9.5 Hz) (-CH_2OAc). Found: C, 65.40; H, 6.81%. Calcd for $C_{28}H_{36}O_9$: C, 65.10; H, 7.03%.

(15*R*)-11,12,16-Triacetoxy-14-hydroxy-8,11,13-abietatriene-6,7-dione (25a) and Its (15*S*)-Isomer (25b). *a*): A solution of **23a** (103.6 mg) in acetone (2.0 ml) was oxidized with Jones reagent (2.5 mol dm^{-3}: 0.40 ml) at 0—5 °C for 5 min and then at room temperature for 2.5 h. The mixture was diluted with ether and washed with water. The dried solution was evaporated in vacuo. The residue was chromatographed on silica gel (10 g), using ether–benzene (1:9) as eluent, to give (15*R*)-coleon D triacetate (**25a**) as an oil (26.9 mg: 27.4%), $[\alpha]_D$ +92.8° (*c* 0.83), IR: 1779, 1732, 1634, and 1606 cm^{-1}; ^1H NMR (90 MHz) δ=1.06 (3H, s), 1.36 (3H, s), and 1.38 (3H, s) (-$C(CH_3)_2$ and C_{10}-CH_3), 1.31 (3H, d, J=7 Hz, C_{15}-CH_3), 1.97 (3H, s, C_{16}-$OCOCH_3$), 2.28 (3H, s) and 2.30 (3H, s) (C_{11}-$OCOCH_3$ and C_{12}-$OCOCH_3$), 3.03 (1H, s, C_5-H), 4.37 (2H, d, J=7 Hz, -CH_2OAc), 13.33 (1H, s, C_{14}-OH). Found: C, 63.63; H, 6.71%. Calcd for $C_{26}H_{32}O_9$: C, 63.92; H, 6.60%.

b): A solution of **23b** (86.5 mg) in acetone (2.0 ml) was oxidized with Jones reagent (2.5 mol dm^{-3}: 0.34 ml) at 0—5 °C for 5 min and then at room temperature for 2.5 h. The crude product was chromatographed on silica gel (7 g), using ether–benzene (1:9) as eluent, to give (15*S*)-coleon D triacetate (**25b**) as an oil (44.5 mg: 54.4%), $[\alpha]_D$ +100.0° (*c* 1.44), IR: 1777, 1733, 1636, and 1610sh cm^{-1}; ^1H NMR (90 MHz) δ=1.05 (3H, s), 1.37 (3H, s), and 1.39 (3H, s) (-$C(CH_3)_2$ and C_{10}-CH_3), 1.32 (3H, d, J=7 Hz, C_{15}-CH_3), 1.97 (3H, s, C_{16}-$OCOCH_3$), 2.28 (3H, s) and 2.30 (3H, s) (C_{11}-$OCOCH_3$ and C_{12}-$OCOCH_3$), 3.02 (1H, s, C_5-H), 4.37 (2H, d, J=7 Hz, -CH_2OAc), 13.31 (1H, s, C_{14}-OH). Found: C, 64.19; H, 6.88%. Calcd for $C_{26}H_{32}O_9$: C, 63.92; H, 6.60%.

(15*R*)-Coleon C (1a) and (15*S*)-Coleon C (1b). *b*): A mixture of **25a** (24.0 mg) and dilute hydrochloric acid (15%: 0.1 ml) in methanol (1.0 ml) was refluxed for 2 h. After the addition of ether, the mixture was washed with brine, dried, and evaporated in vacuo. The residue was chromatographed on silica gel (Mallinckrodt CC-4, 5 g), using hexane–chloroform (3:7) as eluent, to give **1a** (17.6 mg: 98.9%) which was recrystallized from methanol, mp 230—232.5 °C, $[\alpha]_D$ +39.0° (MeOH, *c* 0.21), IR (KBr): 3525, 3350sh, 1623, 1594, and 1576 cm^{-1}; ^1H NMR (90 MHz, acetone-d_6) δ=1.28 (3H, d, J=7 Hz, C_{15}-CH_3), 1.43 (3H, s) and 1.45 (3H, s) (-$C(CH_3)_2$), 1.68 (3H, s, C_{10}-CH_3), 3.89 (1H, dd, J=11 and 2 Hz) and 4.08 (1H, dd, J=11 and 4 Hz) (-CH_2OH), 13.12 (1H, s, C_{14}-OH). Found: C, 66.49; H, 7.15%. Calcd for $C_{20}H_{26}O_6$: C, 66.28; H, 7.23%. The synthetic **1a** was identical with natural (15*R*)-coleon C (mp 236—238 °C, $[\alpha]_D$ +46.8° (MeOH)).[2]

b): A mixture of **25b** (38.8 mg) and dilute hydrochloric acid (15%: 0.15 ml) in methanol (1.5 ml) was refluxed for 1 h. The crude product was chromatographed on silica gel (Mallinckrodt CC-4, 6 g), using hexane–chloroform (3:7) as eluent, to give **1b** (28.7 mg: 99.7%) which was recrystallized from methanol, mp 199.5—201.5 °C, $[\alpha]_D$ −41.0° (MeOH, *c* 0.39), IR (KBr): 3470, 3330sh, 1622, 1596, and 1574 cm^{-1}; ^1H NMR (90 MHz acetone-d_6) δ=1.31 (3H, d, J=7 Hz, C_{15}-CH_3), 1.43 (3H, s) and 1.45 (3H, s) (-$C(CH_3)_2$), 1.68 (3H, s, C_{10}-CH_3), 3.87 (1H, dd, J=11 and 2 Hz) and 4.08 (1H, dd, J=11 and 4 Hz) (-CH_2OH), 13.10 (1H, s, C_{14}-OH). Found: C, 66.53; H, 7.38%. Calcd for $C_{20}H_{26}O_6$: C, 66.28; H, 7.23%. The synthetic **1b** was identical with natural (15*S*)-coleon C (mp 202—204 °C, $[\alpha]_D$ −34.7° (MeOH)).[2]

(15*S*)-Coleon C Tetraacetate (26b). The synthetic **1b** (19.7 mg) was acetylated with acetic anhydride (0.5 ml) in pyridine (0.5 ml) at 75—80 °C for 2 h. The crude product was chromatographed on silica gel (5 g), using ether–benzene (1:9) as eluent, to give **26b** (22.2 mg: 77.1%) which was recrystallized from acetone–hexane, mp 222—224 °C, $[\alpha]_D$ +28.6° (*c* 0.63), IR: 1771, 1729, 1631sh, and 1611 cm^{-1}; ^1H NMR (90 MHz) δ=1.32 (3H, d, J=7 Hz, C_{15}-CH_3), 1.36 (6H, s, -$C(CH_3)_2$), 1.63 (3H, s, C_{10}-CH_3), 1.97 (3H, s, C_{16}-$OCOCH_3$), 2.28 (3H, s), 2.29 (3H, s), and 2.33 (3H, s) (C_6-$OCOCH_3$, C_{11}-$OCOCH_3$, and C_{12}-$OCOCH_3$), 3.37 (1H, m, C_{15}-H), 4.37 (2H, bd, J=7 Hz, -CH_2OAc), 13.51 (1H, s, C_{14}-OH). Found: C, 63.68; H, 6.51%. Calcd for $C_{28}H_{34}O_{10}$: C, 63.38; H, 6.46%.

(15*S*)-11,12-Diacetoxy-14,16-epoxy-6-hydroxy-5,8,11,13-abietatetraen-7-one (27b) and (15*S*)-11,12-Diacetoxy-14,16-epoxy-8,11,13-abietatriene-6,7-dione (28b). A solution of **24b** (86.0 mg) in acetone (3.0 ml) was oxidized with Jones reagent (2.5 mol dm^{-3}: 0.41 ml) at 0—5 °C for 5 min and then at room temperature for 2 h. The crude product was chromatographed on silica gel (10 g), using ether–benzene (1:9) as eluent, to give **27b** (21.9 mg: 24.6%) which was recrystallized from acetone–hexane, mp 248—250 °C, $[\alpha]_D$ +44.6° (*c* 0.56), IR: 3377, 1780, and 1631 cm^{-1}; ^1H NMR (90 MHz) δ=1.24 (3H, d J=7 Hz, C_{15}-CH_3), 1.42 (3H, s) and 1.44 (3H, s) (-$C(CH_3)_2$), 1.56 (3H, s, C_{10}-CH_3), 2.28 (3H, s) and 2.33 (3H, s) (C_{11}-$OCOCH_3$ and C_{12}-$OCOCH_3$), 4.32 (1H, dd, J=7 and 8 Hz) and 4.92 (1H, t, J=9 Hz) (-OCH_2-), 7.22 (1H, s, C_6-OH). Found: C, 67.53; H, 6.81%. Calcd for $C_{24}H_{28}O_7$: C, 67.27; H, 6.59%. Further elution gave a mixture of **27b** and **28b** (11.6 mg: 13.1%). Elution with ether–benzene (1:1) gave **28b** (13.0 mg: 14.6%) which was recrystallized from acetone–hexane, mp 220—223 °C decomp, $[\alpha]_D$ +177.5° (*c* 0.36), IR: 1779, 1747, and 1680 cm^{-1}; ^1H NMR (90 MHz) δ=1.07 (3H, s), 1.43 (3H, s), and 1.46 (3H, s) (-$C(CH_3)_2$ and C_{10}-CH_3), 1.25 (3H, d, J=7 Hz, C_{15}-CH_3), 2.28 (6H, s, C_{11}-$OCOCH_3$ and C_{12}-$OCOCH_3$), 2.54 (1H, bs, C_5-H), 4.32 (1H, dd, J=7 and 8 Hz) and 4.90 (1H, t, J=9 Hz) (-OCH_2-). Found: C, 67.48; H, 6.76%. Calcd for $C_{24}H_{28}O_7$: C, 67.27; H, 6.59%.

The diacetate **27b** (11.6 mg) was refluxed with dilute hydrochloric acid (15%: 0.1 ml) in ethanol (1.0 ml) for 3 h to give a triol **29b**, whose ^1H NMR spectrum showed no signal at δ=10—15 due to a hydrogen-bonded hydroxyl group at the C-14 position.

2-[4-[(*S*)-2-Acetoxy-1-methylethyl]-2,5-dioxo-1(6),3-cyclohexadienyl]-2,6,6-trimethylcyclohexaneacetic Acid (3b). A solution of (15*S*)-12,16-epoxy-8,11,13-abietatriene (**5b**)[4] (132 mg) in acetic acid (3.0 ml) was oxidized with chromium trioxide (69.6 mg) at room temperature for 1 h. The crude product was chromatographed on silica gel (10 g), using benene as eluent, to give (15*S*)-12,16-epoxy-8,11,13-abietatrien-7-one (**6b**) as an oil (87.2 mg: 63.0%), $[\alpha]_D$ +18.4°(*c* 2.99), IR: 1658 cm^{-1}; ^1H NMR δ=0.92 (3H, s) and 0.97 (3H, s)

(-C(CH$_3$)$_2$), 1.20 (3H, s, C$_{10}$-CH$_3$), 1.31 (3H, d, J=7 Hz, C$_{15}$-CH$_3$), 4.08 (1H, dd, J=7 and 9 Hz) and 4.71 (1H, t, J=9 Hz) (-OCH$_2$-), 6.71 (1H, s, C$_{11}$-H), 7.89 (1H, s, C$_{14}$-H). Found: C, 80.28; H, 8.94%. Calcd for C$_{20}$H$_{26}$O$_2$: C, 80.49; H, 8.78%.

According to the method of Burnell et al.,[3] the ketone **6b** (87.2 mg) in acetic anhydride (1.0 ml) was oxidized with peracetic acid prepared from hydrogen peroxide (30%: 0.5 ml), acetic anhydride (1.5 ml), and concentrated sulfuric acid (0.01 ml). The crude product was chromatographed on silica gel (10 g), using hexane–ethyl acetate (7:3 and then 1:1) as eluents, to give **3b** (74.4 mg: 65.2%) which was recrystallized from ethanol, mp 148—150 °C, $[\alpha]_D$ −52.4° (*c* 1.26), IR: 3200, 1726, and 1651 cm^{-1}; ^{1}H NMR δ=0.92 (3H, s) and 0.99 (3H, s) (-C(CH$_3$)$_2$), 1.21 (3H, d, J=7 Hz, C$_{15}$-CH$_3$), 1.29 (3H, s, C$_{10}$-CH$_3$), 2.09 (3H, s, -OCOCH$_3$), 3.76 (1H, dd, J=11 and 4 Hz) and 4.87 (1H, dd, J=11 and 3 Hz) (-CH$_2$OAc), 6.36 (1H, d, J=1.5 Hz, C$_{14}$-H), 6.58 (1H, s, C$_{11}$-H). The physical and spectral data of the synthetic (15*S*)-quinone **3b** were identical with those of the reported major quinone (mp 143—145 °C, $[\alpha]_D$ −50°), whose stereochemistry at the C-15 position was assigned to be R configuration by Burnell et al.[3]

References

1) P. Rüedi and C. H. Eugster, *Helv. Chim. Acta*, **54**, 1606 (1971).

2) P. Rüedi, J. M. Schmid, and C. H. Eugster, *Helv. Chim. Acta*, **65**, 2181 (1982).

3) R. H. Burnell, M. Neron, and S. Savard, *Synth. Commun.*, **12**, 11 (1982); R. H. Burnell, A. Andersen, M. Neron, and S. Savard, *Can. J. Chem.*, **63**, 2769 (1985).

4) T. Matsumoto, S. Imai, T. Yoshinari, and K. Tsuruta, *Bull. Chem. Soc. Jpn.*, **60**, 2401 (1987).

5) T. Matsumoto, S. Imai, and T. Yoshinari, *Bull. Chem. Soc. Jpn.*, **58**, 1165 (1985).