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# The C(1)–C(10) Bond Cleavage and B Ring Aromatization of Some 6-Hydroxy-5$\beta H$-abieta-6,8,11,13-tetraen-18-oic Acid 18,6-Lactones

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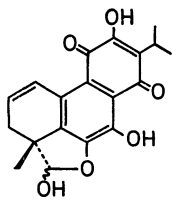
Fusion of 6-hydroxy-5$\beta H$-abieta-6,8,11,13-tetraen-18-oic acid 18,6-lactone (**2**) with potassium hydrogensulfate at 220 °C afforded bis[3-(2,3-dihydro-7-isopropyl-3,4-dimethyl-2-oxonaphtho[2,3-*b*]furan-3-yl)propyl] ether (**12**) in 37% yield, together with two minor products in 12% yield: 2,3-dihydro-7-isopropyl-3,4-dimethyl-3-propylnaphtho[2,3-*b*]furan-2-one and 3-allyl-2,3-dihydro-7-isopropyl-3,4-dimethylnaphtho[2,3-*b*]furan-2-one. Treatment of **12** with *p*-toluenesulfonic acid at 160 °C gave 2,3-dihydro-7-isopropyl-3,4-dimethyl-3-(3-tosyloxypropyl)naphtho[2,3-*b*]furan-2-one, which was converted into 2,3-dihydro-3-(3-hydroxypropyl)-7-isopropyl-3,4-dimethylnaphtho[2,3-*b*]furan-2-one (**16**). The alcohol **16** was further characterized as its acetate (**17**). After several attempts, the above C(1)–C(10) bond cleavage and B ring aromatization reaction were improved by use of concentrated sulfuric acid in refluxing acetic acid. Under these conditions, **2** gave **17** in 47% yield. Hydrolysis of **17** with hydrochloric acid afforded **16**. Subsequently, 12-hydroxy-, 12-methoxy-, 12-acetoxy-, and 12-nitro-6-hydroxy-5$\beta H$-abieta-6,8,11,13-tetraen-18-oic acid 18,6-lactones were each refluxed with concentrated sulfuric acid in acetic acid to give 6-hydroxy-, 6-methoxy-, 6-acetoxy-, and 6-nitro-3-(3-acetoxypropyl)-2,3-dihydro-7-isopropyl-3,4-dimethylnaphtho[2,3-*b*]furan-2-ones, respectively. From the present study, the 12-acetoxy derivative seems to be a suitable intermediate for the synthesis of coleon A.

Coleon A has been isolated from the leaves of *Coleus igniarius* Schweinf. (Labiatae) by Eugster *et al.*[1] On the basis of chemical and spectroscopic studies, they deduced the structure of coleon A to be **1**.[2,3] This is a very unique structure possessing a highly oxygenated 1,10-secoabietane skeleton. During the course of our synthetic studies on natural diterpenes we found[4] that, when 6-hydroxy-5$\beta H$-abieta-6,8,11,13-tetraen-18-oic acid 18,6-lactone (**2**) was treated with potassium hydrogensulfate or concentrated sulfuric acid, the C(1)–C(10) bond cleavage and B ring aromatization occurred. This paper[5] describes a novel synthesis of the coleon A skeleton.

Oxidation[7] of methyl abieta-6,8,11,13-tetraen-18-oate (**3**)[6] in chloroform with perbenzoic acid at room temperature afforded a mixture of the B ring oxygenated products, which was immediately treated with *p*-toluenesulfonic acid monohydrate in refluxing toluene to afford **2**. The IR spectrum of **2** showed bands at 1800 and 1692 $cm^{-1}$ corresponding to a $\gamma$-lactone and a double bond, and its $^1H$ NMR spectrum showed signals at $\delta$ 2.65 (d, $J$=2.5 Hz) and 5.96 (d, $J$=2.5 Hz) due to the C-5 and C-7 protons. The stereochemistry of the C-5 position in **2** was established as follows. Catalytic hydrogenation of **2** in acetic acid over $PtO_2$, followed by esterification with diazomethane yielded the known methyl 5$\beta H$-abieta-8,11,13-trien-18-oate (**4**)[8] (IR: 1725 $cm^{-1}$), together with 6$\alpha$-hydroxy-5$\beta H$-abieta-8,11,13-trien-18-oic acid 18,6$\alpha$-lactone (**5**) (IR: 1758 $cm^{-1}$) and a small amount of its 18,6$\beta$-lactone epimer (**6**) (IR: 1760 $cm^{-1}$); their structures were supported by the following $^1H$ NMR spectra. The spectrum of **5** showed two singlet signals at $\delta$ 1.18 and 1.29 due to the C-10 and C-4 methyls, and signals for the C-5, C-6, and C-7 protons at $\delta$ 2.21 (1H, d, $J$=8.5 Hz), 4.88 (1H, dt, $J$=8.5 and 4 Hz), and 3.06 (2H, d, $J$=4 Hz). These spectral data suggested that **5** exists in a steroidal conformation (**5a**) in which the C(6)–O bond is axial to the twist-boat B ring and the A ring is a chair, as has been reported for 6$\alpha$-hydroxy-5$\beta H$-podocarpa-8,11,13-trien-18-oic acid 18,6$\alpha$-lactone (**7**).[9] While the spectrum of **6** showed the C-4 and C-10 methyl signals at $\delta$ 1.41 (6H), and signals for the C-5, C-6, and C-7 protons at $\delta$ 1.77 (1H, d, $J$=11 Hz), 4.38 (1H, dt, $J$=11 and 5 Hz), and 2.88 (1H, dd, $J$=15

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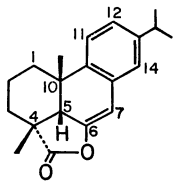


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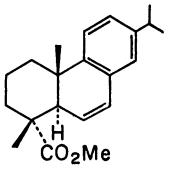


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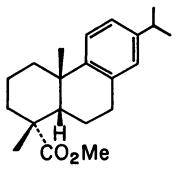


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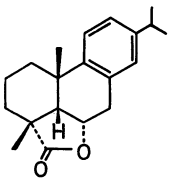


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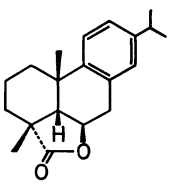


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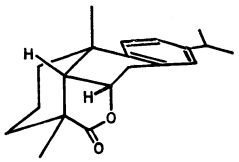
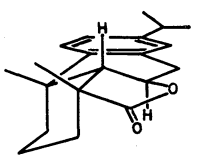
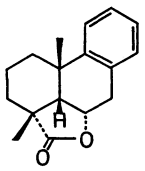


5a



6a



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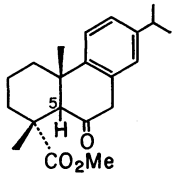


8 5β H
9 5α H

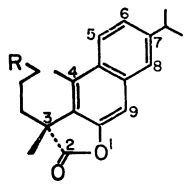
and 11 Hz) and 3.18 (1H, dd, $J$=15 and 5 Hz). These coupling patterns of the protons in the B ring and the chemical shifts of the C-10 methyl which is deshielded by the aromatic C ring, suggested that **6** exists in the nonsteroidal conformation (**6a**).[10] Methanolysis of **2** with concentrated hydrochloric acid in refluxing methanol afforded an A/B *cis* keto ester, methyl 6-oxo-5β*H*-abieta-8,11,13-trien-18-oate (**8**). On the other hand, the corresponding A/B *trans* keto ester, methyl 6-oxoabieta-8,11,13-trien-18-oate (**9**)[11] which was obtained from the above oxidation mixture of **3** with perbenzoic acid, was never epimerized to **8** with concentrated hydrochloric acid in refluxing methanol.

Fusion of **2** with potassium hydrogensulfate at 220 °C for 12 h afforded three naphthalene derivatives (**10**, **11**, and **12**), which were separated by a careful column chromatography on silica gel. The compound **10** was obtained as a minor product (6%) and showed the presence of a naphthalene chromophore in the UV spectrum,[12] an enol γ-lactone moiety in the IR spectrum (1798 $cm^{-1}$), and a molecular weight 296 in the mass spectrum. The $^1H$ NMR spectrum of **10** showed signals due to an isopropyl at δ 1.32 (6H, d, $J$=7 Hz), two methyls at δ 1.59 and 2.61 (each 3H and s), a propyl at δ 0.7—1.25 (5H, m) and 2.05 (2H, m), and four aromatic protons at δ 7.20 (1H, s), 7.26 (1H, dd, $J$=8.5 and 2 Hz), 7.50 (1H, d, $J$= 2 Hz), and 7.82 (1H, d, $J$=8.5 Hz). These spectral data clarified the structure of **10** to be (*R*)-2,3-dihydro-7-isopropyl-3,4-dimethyl-3-propylnaphtho[2,3-*b*]furan-2-one. This structure was further confirmed by the conversion of **10** with dimethyl sulfate in the presence of potassium hydroxide in refluxing acetone to the corresponding methoxy ester (**13**) [IR: 1725 $cm^{-1}$; $^1H$ NMR: δ 3.53 (3H, s, $-CO_2CH_3$) and 3.78 (3H, s, $-OCH_3$)].

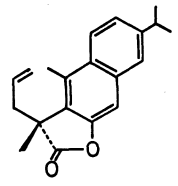
The compound **11** was also obtained as another minor product (6%), whose IR and $^1H$ NMR spectra were very similar to those of **10**, except for the presence of an allyl group [IR: 1633, 987, 910 $cm^{-1}$; $^1H$ NMR: δ 2.79 (2H, d, $J$=6.5 Hz) and 4.75—5.60 (3H, m)] instead of the propyl group in **10**. Catalytic hydrogenation of **11** in methanol over Pd–C gave **10**. Thus, the structure of **11** was assigned as (*R*)-3-allyl-2,3-dihydro-7-isopropyl-3,4-dimethylnaphtho-[2,3-*b*]furan-2-one.

The compound **12** was obtained as a major product (37%); its IR and $^1H$ NMR spectra were also very similar to those of **10**; a molecular weight of 606 was found from the mass spectrum. A triplet signal at δ 3.07 (2H, $J$=6 Hz) in the $^1H$ NMR spectrum suggested the structure of **12** to be a dimer possessing an ether linkage at both the ω-positions of propyl groups in two monomers (**10**). The ether dimer **12** was heated at 160 °C with *p*-toluenesulfonic acid in 1,1,2,2-tetrachloroethane to give (*R*)-2,3-dihydro-7-isopropyl-3,4-dimethyl-3-(3-tosyloxypropyl)-naphtho[2,3-*b*]furan-2-one (**14**) (IR: 1795, 1637, 1360, 1172 $cm^{-1}$), which was converted into the corresponding iodide (**15**) by refluxing with potassium iodide in acetone. Treatment of **15** with potassium *t*-butoxide in dimethyl sulfoxide at room temperature afforded (*R*)-2,3-dihydro-3-(3-hydroxypropyl)-7-isopropyl-3,4-dimethylnaphtho[2,3-*b*]furan-2-one (**16**), together with a small amount of **11**. The alcohol **16** was further characterized as its acetate (**17**) (IR: 1797, 1730, 1640 $cm^{-1}$). The structures of **14**, **15**, **16**, and **17** were also supported by their $^1H$ NMR spectra.[12]

Subsequently, we examined the reaction of **2** with concentrated sulfuric acid to find more effective conditions. Treatment of **2** with concentrated sulfuric acid in refluxing toluene for 2 h gave the tosylate **14** in 17% yield. However, when **2** in acetic acid was refluxed for 3 h with concentrated sulfuric acid, the acetate **17** was obtained in 47% yield. Hydrolysis of **17** with hydrochloric acid in refluxing methanol yielded the alcohol **16**, which was converted into the tosylate **14** by treatment with *p*-toluenesulfonyl chloride in pyridine and into a chloride (**18**)



10 R=H
14 R=OTs
15 R=I
16 R=OH
17 R=OAc
18 R=Cl



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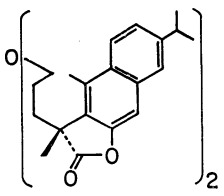

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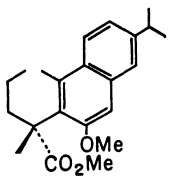


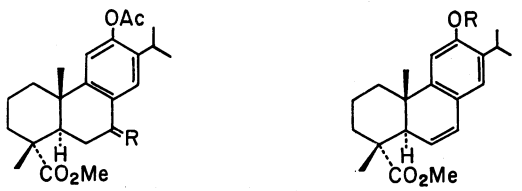
13

by refluxing with triphenylphosphine in carbon tetrachloride.

To obtain further information on the C(1)–C(10) bond cleavage and B ring aromatization leading to a suitable intermediate for the synthesis of coleon A, some C(12)-substituted derivatives of **2** were synthesized. Oxidation of methyl 12-acetoxyabieta-8,11,13-trien-18-oate (**19**)[13,14] with chromium trioxide in aqueous acetic acid afforded methyl 12-acetoxy-7-oxoabieta-8,11,13-trien-18-oate (**20**)[15] which, without purification, was converted into methyl 12-hydroxyabieta-6,8,11,13-tetraen-18-oate (**21**) by reduction with sodium borohydride in methanol, followed by refluxing with *p*-toluenesulfonic acid monohydrate in benzene. The crude hydroxy compound **21** was acetylated with acetic anhydride in pyridine to give methyl 12-acetoxyabieta-6,8,11,13-tetraen-18-oate (**22**), and methylated with methyl iodide in the presence of potassium *t*-butoxide in refluxing *t*-butyl alcohol to give methyl 12-methoxyabieta-6,8,11,13-tetraen-18-oate (**23**). Oxidation of **22** and **23** with perbenzoic acid in chloroform, followed by treatment with *p*-toluenesulfonic acid monohydrate in refluxing toluene, afforded respectively 6,12-dihydroxy-5$\beta H$-abieta-6,8,11,13-tetraen-18-oic acid 18,6-lactone (**24**) and 6-hydroxy-12-methoxy-5$\beta H$-abieta-6,8,11,13-tetraen-18-oic acid 18,6-lactone (**25**). Acetylation of **24** with acetic anhydride in pyridine yielded 12-acetoxy-6-hydroxy-5$\beta H$-abieta-6,8,11,13-tetraen-18-oic acid 18,6-lactone (**26**). The methoxy lactone **25** was also obtained from **24** by methylation with dimethyl sulfate in the presence of anhydrous potassium carbonate in refluxing acetone. Nitration of **2** in acetic anhydride with fuming nitric acid gave 6-hydroxy-12-nitro-5$\beta H$-abieta-6,8,11,13-tetraen-18-oic acid 18,6-lactone (**27**), whose $^1$H NMR spectrum showed two singlet signals at $\delta$ 7.08 and 7.69 due to the two aromatic protons, suggesting that the nitration occurred at the C-12 position in **2**. The $^1$H NMR spectra[12] of **24**, **25**, **26**, and **27** also suggested that the stereochemistry of the C-5 position in these $\gamma$-lactones was identical with that of **2**.

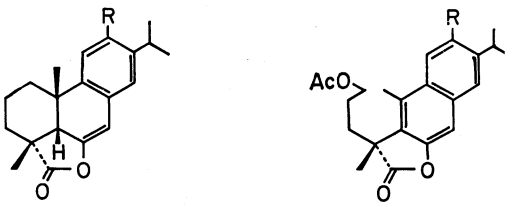
Subsequently, the $\gamma$-lactones were subjected to the C(1)–C(10) bond cleavage and B ring aromatization. The reaction conditions and yields are summarized in Table 1. The hydroxy $\gamma$-lactone **24** in acetic acid was refluxed for 1 h with concentrated sulfuric acid to give (*R*)-3-(3-acetoxypropyl)-2,3-dihydro-6-hydroxy-7-isopropyl-3,4-dimethylnaphtho[2,3-*b*]furan-2-one (**28**) and a small amount of (*R*)-6-acetoxy-3-(3-acetoxypropyl)-2,3-dihydro-7-isopropyl-3,4-dimethylnaphtho-[2,3-*b*]furan-2-one (**29**). Acetylation of **28** with acetic anhydride in pyridine afforded **29**. Similar treatment of **25**, **26**, and **27** also yielded the corresponding 2,3-dihydronaphtho[2,3-*b*]furan-2-one derivatives, **30**, **29**, and **31**, respectively. From the present study, the 12-acetoxy lactone **26** seems to be a useful intermediate for the synthesis of coleon A.

One possible mechanism of the reaction of the 5$\beta H$-$\gamma$-lactones (**2**, **24**, **25**, **26**, and **27**) with concentrated sulfuric acid in refluxing acetic acid would be the following. These lactones should exist in a non-steroidal conformation (**32**), because no steroidal conformation could be constructed with molecular models. The reaction would be initiated by oxidative elimination of an allylic C-5$\beta$ hydrogen atom with concentrated sulfuric acid.[16] Then the C(1)–C(10) bond antiperiplaner to the C(5)–H one is cleaved with a back attack of an acetate anion at the C-1 position. This would stabilize the molecule by the B ring aromatization and by the disappearance of any 1,3-diaxial interaction between the C-4 and C-10 methyl groups.




**19** R=H$_2$
**20** R=O

**21** R=H
**22** R=Ac
**23** R=Me



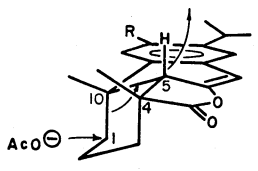

**24** R=OH
**25** R=OMe
**26** R=OAc
**27** R=NO$_2$

**28** R=OH
**29** R=OAc
**30** R=OMe
**31** R=NO$_2$

Table 1. The C(1)-C(10) bond cleavage and B ring aromatization of $\gamma$-lactones

| $\gamma$-Lactone | Refluxing time/h | Product | Yield/% |
|---|---|---|---|
| **2** | 3 | **17** | 47 |
| **24** | 1 | **28**+**29** | 27 |
| **25** | 1 | **30** | 32 |
| **26** | 1.5 | **29** | 42 |
| **27** | 2 | **31** | 16[a] |

a) 64% of **27** was recovered.




**32**

## Experimental

All melting points are uncorrected. The IR and optical rotations were measured in chloroform, and the $^1$H NMR spectra in carbon tetrachloride at 90 MHz, with tetramethylsilane as an internal standard, unless otherwise stated. The

chemical shifts are presented in terms of $\delta$ values; s: singlet, bs: broad singlet, d: doublet, bd: broad doublet, dd: double doublet, t: triplet, dt: double triplet, m: multiplet. The low-resolution mass spectra were obtained by direct inlet (ion-source temperature 200 °C and ionizing voltage 70 eV). The column chromatography was performed using Merck silica gel (0.063 mm).

*6-Hydroxy-5βH-abieta-6,8,11,13-tetraen-18-oic Acid 18,6-Lactone (2).* A solution of perbenzoic acid[17] (38.5 mmol) in chloroform (110 ml) was added to a solution of methyl abieta-6,8,11,13-tetraen-18-oate (**3**)[6] (10.8 g, 34.6 mmol) in chloroform (80 ml) at room temperature. After standing at room temperature for 24 h, the solution was diluted with ether (500 ml), and washed successively with aqueous potassium iodide, aqueous sodium thiosulfate, aqueous sodium hydrogencarbonate, and brine. The organic solution was dried over sodium sulfate and evaporated *in vacuo* to give yellowish brown oil (13.2 g).

This oil (13.2 g) was immediately refluxed with *p*-toluenesulfonic acid monohydrate (5.6 g) in toluene (260 ml) for 3 h, cooled, and diluted with ether (250 ml). The solution was washed successively with aqueous sodium hydrogencarbonate and brine, dried over sodium sulfate, and evaporated *in vacuo*. The residual brown oil (10.5 g) was crystallized from hexane to afford **2** (6.4 g) as colorless needles, mp 106—107 °C. The mother liquor of crystallization was evaporated and the residue was chromatographed on silica gel (410 g), using hexane–benzene (1:1) as the eluent, to give some additional **2**, which was crystallized from hexane to give colorless crystals (0.9 g), mp 105—106 °C. The total yield was 70%. Further crystallization gave an analytical sample; mp 106.5—107 °C; $[\alpha]_D$ −116° (*c* 1.54); IR: 1800, 1692 $cm^{-1}$; $^1H$ NMR: 1.22 (6H, d, $J$=7 Hz, $-CH(C\underline{H}_3)_2$), 1.46 and 1.52 (each 3H and s, $C_4$–$CH_3$ and $C_{10}$–$CH_3$), 2.65 (1H, d, $J$=2.5 Hz, $C_{5\beta}$–H), 2.80 (1H, m, $-C\underline{H}(CH_3)_2$), 5.96 (1H, d, $J$=2.5 Hz, $C_7$–H), 6.78 (1H, d, $J$=2 Hz, $C_{14}$–H), 6.89 (1H, dd, $J$=8 and 2 Hz, $C_{12}$–H), 7.08 (1H, d, $J$=8 Hz, $C_{11}$–H); UV: $\lambda_{max}^{EtOH}$ 271 nm (log $\varepsilon$ 4.07), 277 (4.07). Found: C, 80.89; H, 8.19%. Calcd for $C_{20}H_{24}O_2$: C, 81.04; H, 8.16%.

*Catalytic Hydrogenation of 2.* A mixture of **2** (5.93 g) and $PtO_2$ (600 mg) in acetic acid (180 ml) was submitted to catalytic hydrogenation with 1 atm hydrogen pressure at room temperature for *ca.* 100 min. After the usual work-up, the crude product was treated with an ethereal diazomethane solution at room temperature for several hours. The solvent was evaporated *in vacuo* and the residue was chromatographed on silica gel (300 g), using hexane–benzene (1:1) at the eluent, to give methyl 5β*H*-abieta-8,11,13-trien-18-oate (**4**)[8] (3.10 g: 49%); $[\alpha]_D$ −79° (*c* 7.35); IR: 1725 $cm^{-1}$; $^1H$ NMR: 1.21 (6H, d, $J$=7 Hz, $-CH(C\underline{H}_3)_2$), 1.31 (6H, s, $C_4$–$CH_3$ and $C_{10}$–$CH_3$), 3.24 (3H, s, $-CO_2CH_3$), 6.76 (1H, bs, $C_{14}$–H), 6.89 (1H, dd, $J$=8 and 2 Hz, $C_{12}$–H), 7.08 (1H, d, $J$=8 Hz, $C_{11}$–H); $^1H$ NMR in $CDCl_3$: 1.22 (6H, d, $J$=7 Hz, $-CH(C\underline{H}_3)_2$), 1.38 (6H, s, $C_4$–$CH_3$ and $C_{10}$–$CH_3$), 3.42 (3H, s, $-CO_2CH_3$). Found: C, 80.50; H, 9.78%. Calcd for $C_{21}H_{30}O_2$: C, 80.21; H, 9.62%.

Subsequent elution with ether–benzene (1:99) afforded 6β-hydroxy-5β*H*-abieta-8,11,13-trien-18-oic acid 18,6β-lactone (**6**), which was recrystallized from hexane to give colorless crystals (29 mg: 0.5%); mp 133—134 °C; $[\alpha]_D$ −90° (*c* 0.335); IR: 1760 $cm^{-1}$; $^1H$ NMR: 1.22 (6H, d, $J$=7 Hz, $-CH(C\underline{H}_3)_2$), 1.41 (6H, s, $C_4$–$CH_3$ and $C_{10}$–$CH_3$), 1.77 (1H, d, $J$=11 Hz, $C_{5\beta}$–H), 2.80 (1H, m, $-C\underline{H}(CH_3)_2$), 2.88 (1H, dd, $J$=15 and 11 Hz, $C_{7\beta}$–H), 3.18 (1H, dd, $J$=15 and 5 Hz, $C_{7\alpha}$–H), 4.38 (1H, dt, $J$=11 and 5 Hz, $C_{6\alpha}$–H), 6.87 (1H, bs, $C_{14}$–H), 6.97 (1H, dd, $J$=8 and 2 Hz, $C_{12}$–H), 7.07 (1H, d, $J$=8 Hz, $C_{11}$–H). Found: C, 80.76; H, 8.87%. Calcd for $C_{20}H_{26}O_2$: C, 80.49; H, 8.78%.

Further elution with the same solvent afforded 6α-hydroxy-5β*H*-abieta-8,11,13-trien-18-oic acid 18,6α-lactone (**5**), which was recrystallized from hexane to give colorless crystals (1.80 g: 30%); mp 109—109.5 °C; $[\alpha]_D$ −45° (*c* 1.21); IR: 1758 $cm^{-1}$; $^1H$ NMR: 1.18 and 1.29 (each 3H and s, $C_{10}$–$CH_3$ and $C_4$–$CH_3$), 1.24 (6H, d, $J$=7 Hz, $-CH(C\underline{H}_3)_2$), 2.21 (1H, d, $J$=8.5 Hz, $C_{5\beta}$–H), 2.83 (1H, m, $-C\underline{H}(CH_3)_2$), 3.06 (2H, d, $J$=4 Hz, $C_7$–$H_2$), 4.88 (1H, dt, $J$=8.5 and 4 Hz, $C_{6\beta}$–H), 6.9—7.1 (3H, m, $C_{11}$–H, $C_{12}$–H, and $C_{14}$–H). Found: C, 80.45; H, 8.88%. Calcd for $C_{20}H_{26}O_2$: C, 80.49; H, 8.78%.

*Methanolysis of 2.* A mixture of **2** (297 mg) and concentrated hydrochloric acid (0.15 ml) in methanol (15 ml) was refluxed for 1 h, and evaporated *in vacuo*. The residue was dissolved in ether and the ether solution was successively washed with sodium hydrogencarbonate and brine. After drying over sodium sulfate, the solvent was evaporated *in vacuo* and the residue was chromatographed on silica gel (33 g), using benzene as the eluent, to give the starting **2** (15 mg: 5%). Further elution with ether–benzene (1:99) gave methyl 6-oxo-5β*H*-abieta-8,11,13-trien-18-oate (**8**) (265 mg: 81%), which was recrystallized from hexane; mp 126—127 °C; $[\alpha]_D$ +36° (*c* 2.59); IR: 1723, 1700 $cm^{-1}$; $^1H$ NMR: 1.09 and 1.18 (each 3H and s, $C_{10}$–$CH_3$ and $C_4$–$CH_3$), 1.23 (6H, d, $J$=7 Hz, $-CH(C\underline{H}_3)_2$), 2.04 (1H, s, $C_{5\beta}$–H), 2.82 (1H, m, $-C\underline{H}(CH_3)_2$), 2.90 (3H, s, $-CO_2CH_3$), 3.44 (2H, s, $C_7$–$H_2$), 6.84 (1H, bs, $C_{14}$–H), 6.99 (1H, dd, $J$=8 and 2 Hz, $C_{12}$–H), 7.12 (1H, d, $J$=8 Hz, $C_{11}$–H). Found: C, 76.50; H, 8.56%. Calcd for $C_{21}H_{28}O_3$: C, 76.79; H, 8.59%.

*Methyl 6-Oxoabieta-8,11,13-trien-18-oate (9).* Chromatographic purification of the crude oxidation product of **3** with perbenzoic acid afforded **9** in *ca.* 30% yield; $[\alpha]_D$ +156° (*c* 1.93); IR: 1720, 1705 $cm^{-1}$; $^1H$ NMR: 1.18 (3H, s, $C_{10}$–$CH_3$), 1.24 (6H, d, $J$=7 Hz, $-CH(C\underline{H}_3)_2$), 1.44 (3H, s, $C_4$–$CH_3$), 2.87 (1H, m, $-C\underline{H}(CH_3)_2$), 3.15 (1H, s, $C_{5\alpha}$–H), 3.52 (2H, s, $C_7$–$H_2$), 3.58 (3H, s, $-CO_2CH_3$), 6.90 (1H, bs, $C_{14}$–H), 7.01 (1H, bd, $J$=8 Hz, $C_{12}$–H), 7.17 (1H, d, $J$=8 Hz, $C_{11}$–H). Found: C, 76.80; H, 8.38%. Calcd for $C_{21}H_{28}O_3$: C, 76.79; H, 8.59%.

A mixture of **9** (300 mg) and concentrated hydrochloric acid (0.15 ml) in methanol (15 ml) was refluxed for 1 h. The same work-up as described for the methanolysis of **2** gave an oil (270 mg), whose IR and $^1H$ NMR spectra showed that it was almost the recovered **9** and did not contain the 5β*H*-epimer (**8**).

*Fusion of 2 with Potassium Hydrogensulfate.* A mixture of **2** (13.31 g) and potassium hydrogensulfate (91.58 g) was heated at 220 °C for 12 h with stirring under a stream of nitrogen. The mixture was cooled, diluted with water, and extracted with ether. The ether extract was washed successively with aqueous sodium hydrogencarbonate and brine, dried over sodium sulfate, and evaporated *in vacuo* The residue was chromatographed on silica gel (800 g), using hexane–benzene (3:2) as the eluent, to give a mixture of naphtho[2,3-*b*]furan-2-one derivatives (3.13 g), whose purification is described later. Subsequent elution with the same solvent recovered the **2** (3.66 g: 27%).

Further elution with ether–benzene (3:97) afforded bis-[3-(2,3-dihydro-7-isopropyl-3,4-dimethyl-2-oxonaphtho[2,3-*b*]furan-3-yl)propyl] ether (**12**) (5.08 g: 37%) as an oil; $[\alpha]_D$ +45° (*c* 1.59); IR: 1780, 1635 $cm^{-1}$; $^1H$ NMR: *ca.* 1.1 (4H, m, $2\text{-}CH_2C\underline{H}_2CH_2O$–), 1.31 (12H, d, $J$=7 Hz, $2\text{-}CH(C\underline{H}_3)_2$), 1.58 (6H, s, $2C_3$–$CH_3$), *ca.* 2.1 (4H, m, $2\text{-}C\underline{H}_2CH_2CH_2O$–), 2.59 (6H, s, $2C_4$–$CH_3$), 3.00 (2H, m, 2-

CH(CH$_3$)$_2$), 3.07 (4H, t, $J$=6 Hz, 2-CH$_2$CH$_2$CH$_2$O-), 7.13 (2H, s, 2C$_9$-H), 7.26 (2H, dd, $J$=9 and 2 Hz, 2C$_6$-H), 7.47 (2H, d, $J$=2 Hz, 2C$_8$-H), 7.83 (2H, d, $J$=9 Hz, 2C$_5$-H); MS (*m/e*): 606 (M$^+$); UV: $\lambda_{max}^{EtOH}$ 235 nm (log $\varepsilon$ 5.14), 271sh (4.05), 281.5 (4.08), 292sh (3.93), 312 (3.29), 326.5 (3.36). Found: C, 79.24; H, 7.81%. Calcd for $C_{40}H_{46}O_5$: C, 79.17; H, 7.64%.

The above mixture of naphtho[2,3-*b*]furan-2-one derivatives (3.13 g) was further purified by repeated column chromatography on silica gel.

The less polar fraction gave (*R*)-2,3-dihydro-7-isopropyl-3,4-dimethyl-3-propylnaphtho[2,3-*b*]furan-2-one (**10**) (0.80 g: 6%), which was recrystallized from hexane; mp 130—130.5 °C, $[\alpha]_D$ +81° (*c* 1.52); IR: 1798, 1642, 1595, 1508 cm$^{-1}$; UV: $\lambda_{max}^{EtOH}$ 235.5 nm (log $\varepsilon$ 4.80), 281.5 (3.76), 293sh (3.63), 312 (3.07), 320sh (2.90), 327 (3.08): $^1$H NMR: 0.7—1.25 (5H, m, -CH$_2$CH$_2$CH$_3$), 1.32 (6H, d, $J$=7 Hz, -CH(CH$_3$)$_2$), 1.59 (3H, s, C$_3$-CH$_3$), *ca.* 2.05 (2H, m, -CH$_2$CH$_2$CH$_3$), 2.61 (3H, s, C$_4$-CH$_3$), 7.20 (1H, s, C$_9$-H), 7.26 (1H, dd, $J$=8.5 and 2 Hz, C$_6$-H), 7.50 (1H, d, $J$=2 Hz, C$_8$-H), 7.82 (1H, d, $J$=8.5 Hz, C$_5$-H; 18% NOE enhancement was observed on irradiation of the signal at $\delta$ 2.61); MS (*m/e*): 296 (M$^+$). Found: C, 81.21; H, 8.18%. Calcd for $C_{20}H_{24}O_2$: C, 81.04; H, 8.16%.

The more polar fraction gave (*R*)-3-allyl-2,3-dihydro-7-isopropyl-3,4-dimethylnaphtho[2,3-*b*]furan-2-one (**11**) (0.83 g: 6%), which was recrystallized from hexane; mp 118—119 °C; $[\alpha]_D$ +130° (*c* 1.25); IR: 1792, 1633, 987, 910 cm$^{-1}$; $^1$H NMR: 1.35 (6H, d, $J$=6.5 Hz, -CH(CH$_3$)$_2$), 1.64 (3H, s, C$_3$-CH$_3$), 2.67 (3H, s, C$_4$-CH$_3$), 2.79 (2H, d, $J$=6.5 Hz, -CH$_2$CH=CH$_2$), 3.04 (1H, m, -CH(CH$_3$)$_2$), 4.75—5.60 (3H, m, -CH$_2$CH=CH$_2$), 7.22 (1H, s, C$_9$-H), 7.29 (1H, dd, $J$=9 and 2 Hz, C$_6$-H), 7.52 (1H, d, $J$=2 Hz, C$_8$-H), 7.86 (1H, d, $J$=9 Hz, C$_5$-H; 18% NOE enhancement was observed on irradiation of the signal at $\delta$ 2.67). Found: C, 81.64; H, 7.61%. Calcd for $C_{20}H_{22}O_2$: C, 81.60; H, 7.53%.

*Catalytic Hydrogenation of* ***11***. A mixture of **11** (122 mg) and 5% Pd-C (25 mg) in methanol (6.0 ml) was subjected to catalytic hydrogenation at room temperature. After the usual work-up, the crude product was recrystallized from hexane to give a dihydro derivative (95 mg: 77%), mp 129—130 °C, whose IR and $^1$H NMR spectra were identical with those of **10**.

*(R)-7-Isopropyl-2-methoxy-3-(1-methoxycarbonyl-1-methylbutyl)-4-methylnaphthalene (**13**).* Dimethyl sulfate (7.5 ml) and 50% aqueous potassium hydroxide (15.5 ml) were added to a stirred solution of **10** (119 mg) in refluxing acetone (15 ml) over a period of 63 min. After addition of acetone (6.0 ml), the mixture was further refluxed for 90 min, diluted with water, neutralized with dilute hydrochloric acid, and then extracted with ether. The ether extract was washed with water, dried over sodium sulfate, and evaporated *in vacuo*. The residue was chromatographed on silica gel (20 g), using benzene as the eluent, to give **13** (68 mg: 50%) as an oil; $[\alpha]_D$ −31° (*c* 1.44); IR: 1725, 1627, 1605 cm$^{-1}$; $^1$H NMR: 0.88 (3H, t, $J$=6.5 Hz, -CH$_2$CH$_2$CH$_3$), *ca.* 1.25 (2H, m, -CH$_2$CH$_2$CH$_3$), 1.30 (6H, d, $J$=7 Hz, -CH(CH$_3$)$_2$), 1.67 (3H, s, C$_3$-C(CH$_3$)-), *ca.* 2.05 (2H, m, C$_3$-C(CH$_2$)-), 2.63 (3H, s, C$_4$-CH$_3$), 2.98 (1H, m, -CH(CH$_3$)$_2$), 3.53 (3H, s, -CO$_2$CH$_3$), 3.78 (3H, s, -OCH$_3$), 6.86 (1H, s, C$_1$-H; 28% NOE enhancement was observed on irradiation of the signal at $\delta$ 3.78), 7.14 (1H, dd, $J$=9 and 2 Hz, C$_6$-H), 7.37 (1H, d, $J$=2 Hz, C$_8$-H), 7.83 (1H, d, $J$=9 Hz, C$_5$-H; 22% NOE enhancement was observed on irradiation of the signal at $\delta$ 2.63). Found: C, 76.97; H, 8.81%. Calcd for $C_{22}H_{30}O_3$: C, 77.15; H, 8.83%.

*(R)-2,3-Dihydro-7-isopropyl-3,4-dimethyl-3-(3-tosyloxypropyl)-naphtho[2,3-b]furan-2-one (**14**).* A solution of **12** (330 mg) in 1,1,2,2-tetrachloroethane (5.0 ml) was added to *p*-toluenesulfonic acid which was prepared from the monohydrate (270 mg) and 1,1,2,2-tetrachloroethane (5.0 ml) by azeotropic distillation. The mixture was stirred at 160 °C for 12 h under a stream of nitrogen, cooled, and diluted with ether. The ether solution was washed with aqueous sodium hydrogencarbonate and brine, dried over sodium sulfate, and evaporated *in vacuo*. The residue was purified by column chromatography on silica gel (55 g), using benzene as the eluent, to give **14** (232 mg: 45%); $[\alpha]_D$ +69° (*c* 2.13); IR: 1795, 1637, 1360, 1172 cm$^{-1}$; $^1$H NMR: *ca.* 1.2 (2H, m, -CH$_2$CH$_2$CH$_2$OTs), 1.31 (6H, d, $J$=7 Hz, -CH(CH$_3$)$_2$), 1.54 (3H, s, C$_3$-CH$_3$), *ca.* 2.05 (2H, m, -CH$_2$CH$_2$CH$_2$OTs), 2.33 (3H, s, -C$_6$H$_4$CH$_3$), 2.57 (3H, s, C$_4$-CH$_3$), 3.01 (1H, m, -CH(CH$_3$)$_2$), 3.77 (2H, t, $J$=6 Hz, -CH$_2$CH$_2$CH$_2$OTs), 7.14 (2H, d, $J$=8 Hz, aromatic protons of *p*-tosyl group), 7.16 (1H, s, C$_9$-H), 7.28 (1H, dd, $J$=8.5 and 2 Hz, C$_6$-H), 7.50 (1H, d, $J$=2 Hz, C$_8$-H), 7.58 (2H, d, $J$=8 Hz, aromatic protons of *p*-tosyl group), 7.84 (1H, d, $J$=8.5 Hz, C$_5$-H); UV: $\lambda_{max}^{EtOH}$ 234 nm (log $\varepsilon$ 4.86), 269.5 (3.80), 273.5 (3.81), 281 (3.80), 293sh (3.65), 312.5 (3.07), 318sh (2.92), 326 (3.10). Found: C, 69.66; H, 6.61%. Calcd for $C_{27}H_{30}O_5S$: C, 69.51; H, 6.48%.

Further elution with ether–benzene (3:97) gave the recovered **12** (117 mg: 34%).

*(R)-2,3-Dihydro-3-(3-iodopropyl)-7-isopropyl-3,4-dimethylnaphtho[2,3-b]furan-2-one (**15**).* A mixture of **14** (362 mg), potassium iodide (791 mg), and acetone (13 ml) was refluxed for 5 h in a dark place. After the solvent had been evaporated *in vacuo*, the residue was mixed with water, and extracted with ether. The ether extract was washed with water, dried over sodium sulfate, and evaporated *in vacuo*. The residual oil was chromatographed on silica gel (35 g), using hexane–benzene (2:1) as the eluent, to give **15** (291 mg: 89%) as an oil; $[\alpha]_D$ +19° (*c* 2.91); IR: 1790, 1632 cm$^{-1}$; $^1$H NMR: 1.33 (6H, d, $J$=7 Hz, -CH(CH$_3$)$_2$), *ca.* 1.4 (2H, m, -CH$_2$CH$_2$CH$_2$I), 1.64 (3H, s, C$_3$-CH$_3$), *ca.* 2.2 (2H, m, -CH$_2$CH$_2$CH$_2$I), 2.69 (3H, s, C$_4$-CH$_3$), 3.03 (2H, t, $J$=6 Hz, -CH$_2$CH$_2$CH$_2$I), 3.03 (1H, m, -CH(CH$_3$)$_2$), 7.18 (1H, s, C$_9$-H), 7.27 (1H, dd, $J$=8 and 2 Hz, C$_6$-H), 7.49 (1H, d, $J$=2 Hz, C$_8$-H), 7.82 (1H, d, $J$=8 Hz, C$_5$-H).

*Reaction of* ***15*** *with Potassium* t*-Butoxide in Dimethyl Sulfoxide.* A solution of potassium *t*-butoxide (560 mg) in dimethyl sulfoxide (5.0 ml) was added to a stirred solution of **15** (200 mg) in dry benzene (3.0 ml). After being stirred overnight at room temperature under a stream of nitrogen, the mixture was diluted with water, acidified with dilute hydrochloric acid, and extracted with ether. The ether extract was washed with water, dried over sodium sulfate, and evaporated *in vacuo*. The residue was chromatographed on silica gel (20 g), using hexane–benzene (1:2) as the eluent, to give a solid (9 mg: 6%) whose IR and $^1$H NMR spectra were identical with those of **11**.

Subsequent elution with ether–benzene (1:3) yielded (*R*)-2,3-dihydro-3-(3-hydroxypropyl)-7-isopropyl-3,4-dimethylnaphtho[2,3-*b*]furan-2-one (**16**) (37 mg: 25%); $[\alpha]_D$ +50° (*c* 0.875); IR: 3620, 3450br, 1795, 1637 cm$^{-1}$; $^1$H NMR: *ca.* 1.1 (2H, m, -CH$_2$CH$_2$CH$_2$OH), 1.32 (6H, d, $J$=7 Hz, -CH(CH$_3$)$_2$), 1.59 (3H, s, C$_3$-CH$_3$), 1.82 (1H, bs, -OH; disappeared with D$_2$O), *ca.* 2.1 (2H, m, -CH$_2$CH$_2$CH$_2$OH), 2.61 (3H, s, C$_4$-CH$_3$), 3.02 (1H, m, -CH(CH$_3$)$_2$), 3.33 (2H, t, $J$=6 Hz, -CH$_2$CH$_2$CH$_2$OH), 7.21 (1H, s, C$_9$-H), 7.27 (1H, dd, $J$=9 and 2 Hz, C$_6$-H), 7.51 (1H, d, $J$=2 Hz,

$C_8$–H), 7.84 (1H, d, $J$=9 Hz, $C_5$–H). Found: C, 77.17; H, 7.93%, Calcd for $C_{20}H_{24}O_3$: C, 76.89; H, 7.74%.

*(R)-3-(3-Acetoxypropyl)-2,3-dihydro-7-isopropyl-3,4-dimethylnaphtho[2,3-b]furan-2-one (**17**).* A mixture of **16** (67 mg), acetic anhydride (0.13 ml), and pyridine (0.34 ml) was allowed to stand overnight at room temperature. After the usual work-up, the crude product was purified by column chromatography on silica gel (7.0 g), using benzene as the eluent, to give **17** (70 mg: 92%) as an oil; $[\alpha]_D$ +11° ($c$ 3.75); IR: 1797, 1730, 1640 $cm^{-1}$; $^1H$ NMR: *ca.* 1.2 (2H, m, $-CH_2C\underline{H}_2CH_2OAc$), 1.33 (6H, d, $J$=7 Hz, $-CH(C\underline{H}_3)_2$), 1.62 (3H, s, $C_3$–$CH_3$), 1.91 (3H, s, $-OCOCH_3$), *ca.* 2.1 (2H, m, $-C\underline{H}_2CH_2CH_2OAc$), 2.62 (3H, s, $C_4$–$CH_3$), 3.01 (1H, m, $-C\underline{H}(CH_3)_2$), 3.83 (2H, t, $J$=6 Hz, $-CH_2CH_2C\underline{H}_2OAc$), 7.20 (1H, s, $C_9$–H), 7.26 (1H, dd, $J$=8 and 2 Hz, $C_6$–H), 7.49 (1H, d, $J$=2 Hz, $C_8$–H), 7.81 (1H, d, $J$=8 Hz, $C_5$–H); UV: $\lambda_{max}^{EtOH}$ 235.5 nm (log $\varepsilon$ 4.83), 281.5 (3.78), 293sh (3.62), 313 (2.95), 327 (3.03). Found: C, 74.51; H, 7.46%. Calcd for $C_{22}H_{26}O_4$: C, 74.55; H, 7.39%.

*Reaction of **2** with Concentrated Sulfuric Acid in Toluene.* A stirred mixture of **2** (297 mg), concentrated sulfuric acid (0.33 ml), and toluene (6.0 ml) was refluxed for 2 h. The mixture was cooled, diluted with water, and extracted with ether, The ether extract was washed successively with brine, aqueous sodium hydrogencarbonate, and brine. After drying over sodium sulfate, the solvent was evaporated *in vacuo* and the residue was purified by column chromatography on silica gel (31 g), using benzene as the eluent, to give an oil (78 mg: 17%) whose IR and $^1H$ NMR spectra were identical with those of **14**.

*Reaction of **2** with Concentrated Sulfuric Acid in Acetic Acid.* A stirred mixture of **2** (148 mg) and concentrated sulfuric acid (0.75 ml) in acetic acid (7.5 ml) was refluxed for 3 h. The reaction mixture was cooled, diluted with water, and extracted with ether. The ether extract was washed successively with water, aqueous sodium hydrogencarbonate, and brine. After drying over sodium sulfate, the solvent was evaporated *in vacuo*. The residue was chromatographed on silica gel (16 g), using benzene as the eluent, to give an oil (83 mg: 47%) whose IR and $^1H$ NMR spectra were identical with those of **17**.

*Hydrolysis of **17**.* A mixture of **17** (354 mg) and concentrated hydrochloric acid (0.5 ml) in methanol (14 ml) was refluxed for 1 h. After the solvent had been evaporated *in vacuo*, the residue was diluted with water and extracted with ether. The ether extract was washed successively with aqueous sodium hydrogencarbonate and brine, dried over sodium sulfate, and evaporated *in vacuo* to give an oil (306 mg) whose IR and $^1H$ NMR spectra were identical with those of **16**.

*Reaction of **16** with* p-*Toluenesulfonyl Chloride.* A mixture of **16** (320 mg) and *p*-toluenesulfonyl chloride (229 mg) in pyridine (1.6 ml) was allowed to stand overnight at room temperature. After the usual work-up, the crude product was chromatographed on silica gel (32 g), using hexane–benzene (1:1) as the eluent, to give (*R*)-3-(3-chloropropyl)-2,3-dihydro-7-isopropyl-3,4-dimethylnaphtho[2,3-*b*]furan-2-one (**18**) (44 mg: 13%), which was recrystallized from hexane; mp 63—65.5 °C; $[\alpha]_D$ +10° ($c$ 0.965); $^1H$ NMR: *ca.* 1.4 (2H, m, $-CH_2C\underline{H}_2CH_2Cl$), 1.33 (6H, d, $J$=7 Hz, $-CH(C\underline{H}_3)_2$), 1.63 (3H, s, $C_3$–$CH_3$), *ca.* 2.25 (2H, m, $-C\underline{H}_2CH_2CH_2Cl$), 2.64 (3H, s, $C_4$–$CH_3$), 3.02 (1H, m, $-C\underline{H}(CH_3)_2$), 3.35 (2H, t, $J$=6 Hz, $-CH_2CH_2C\underline{H}_2Cl$), 7.20 (1H, s, $C_9$–H), 7.26 (1H, dd, $J$=9 and 2 Hz, $C_6$–H), 7.48 (1H, d, $J$=2 Hz, $C_8$–H), 7.82 (1H, d, $J$=9 Hz, $C_5$–H); MS (*m/e*): 332 ($M^+$+2), 330 ($M^+$). Found: C, 72.84; H, 7.30%. Calcd for $C_{20}H_{23}O_2Cl$: C, 72.61; H, 7.01%.

Subsequent elution with benzene afforded a tosylate (228 mg: 49%) whose IR and $^1H$ NMR spectra were identical with those of **14**.

Further elution with ether–benzene (15:85) recovered some of the **16** (32 mg: 10%).

*(R)-3-(3-Chloropropyl)-2,3-dihydro-7-isopropyl-3,4-dimethylnaphtho[2,3-b]furan-2-one (**18**).* A mixture of **16** (312 mg) and triphenylphosphine (290 mg) in carbon tetrachloride (2.0 ml) was refluxed for 4 h. The solvent was removed *in vacuo* and the residue was purified by column chromatography on silica gel (55 g), using hexane–benzene (1:1) as the eluent, to give a solid (275 mg: 83%) whose IR and $^1H$ NMR spectra were identical with those of **18**.

*Methyl 12-Acetoxyabieta-6,8,11,13-tetraen-18-oate (**22**).* A solution of chromium trioxide (30 g) in 80% aqueous acetic acid (150 ml) was added dropwise to a stirred solution of methyl 12-acetoxyabieta-8,11,13-trien-18-oate (**19**)[13,14] (37.2 g) in acetic acid (560 ml) at 20—25 °C over a period of 1 h. The mixture was stirred at this temperature for 18 more h, poured into water, and extracted with chloroform. The chloroform extract was washed successively with aqueous sodium hydrogencarbonate and brine, dried over sodium sulfate, and evaporated *in vacuo* to give methyl 12-acetoxy-7-oxoabieta-8,11,13-trien-18-oate (**20**);[15] IR: 1755, 1725, 1678, 1612 $cm^{-1}$; $^1H$ NMR: 6.90 (1H, s, $C_{11}$–H), 7.87 (1H, s, $C_{14}$–H).

The above crude 7-oxo compound (**20**) (40 g), without purification, was allowed to reduce overnight with sodium borohydride (5.7 g) in methanol (400 ml) at room temperature. After removal of the solvent *in vacuo*, the residue was diluted with water (1.5 l) and acidified with dilute hydrochloric acid. The precipitates were collected, washed with water, and dried at 80—90 °C to yield a mixture of epimeric 7-hydroxy compounds as a solid which, without purification, was used in the next reaction.

This dried solid (36.5 g) in benzene (1.5 l) was refluxed with *p*-toluenesulfonic acid monohydrate (1.8 g) for 2 h. The mixture was concentrated *in vacuo* to a half volume, cooled, and diluted with ether (750 ml). The ether solution was washed successively with aqueous sodium hydrogencarbonate and water, dried over sodium sulfate, and evaporated *in vacuo* to give the crude methyl 12-hydroxyabieta-6,8,11,13-tetraen-18-oate (**21**); IR: 3600, 3330br, 1722 $cm^{-1}$; $^1H$ NMR: 2.76 (1H, t, $J$=2.5 Hz, $C_{5\alpha}$–H), 5.47 and 6.34 (each 1H and dd, $J$=10 and 2.5 Hz, $C_6$–H and $C_7$–H), 6.47 and 6.72 (each 1H and s, $C_{11}$–H and $C_{14}$–H).

The crude 12-hydroxy compound (**21**) (32 g) was acetylated with acetic anhydride (32 ml) in pyridine (96 ml) at room temperature for 1 h. After the usual work-up, the crude product was purified by column chromatography on silica gel (350 g), using benzene as the eluent, to give **22** (26.9 g: 73% from **19**) as an oil; $[\alpha]_D$ −19° ($c$ 1.89); IR: 1748, 1715 $cm^{-1}$; $^1H$ NMR: 1.08 (3H, s, $C_{10}$–$CH_3$), 1.34 (3H, s, $C_4$–$CH_3$), 2.22 (3H, s, $-OCOCH_3$), 2.84 (1H, t, $J$=2.5 Hz, $C_{5\alpha}$–H), 3.60 (3H, s, $-CO_2CH_3$), 5.66 and 6.43 (each 1H and dd, $J$=10 and 2.5 Hz, $C_6$–H and $C_7$–H), 6.68 and 6.89 (each 1H and s, $C_{11}$–H and $C_{14}$–H). Found: C, 74.50; H, 8.10%. Calcd for $C_{23}H_{30}O_4$: C, 74.56; H, 8.16%.

*Methyl 12-Methoxyabieta-6,8,11,13-tetraen-18-oate (**23**).* A mixture of the above crude **21** (3.3 g) and potassium *t*-butoxide (1.35 g) in *t*-butyl alcohol (44 ml) was stirred at room temperature for 10 min and methyl iodide (2.82 g) was added dropwise over a 5 min period. The mixture was refluxed for 2 h and evaporated *in vacuo*. The residue was diluted with water, acidified with dilute hydrochloric acid, and extracted with ether. The ether extract was

washed with water, dried over sodium sulfate, and evaporated *in vacuo*. The crude product was chromatographed on silica gel (200 g), using benzene as the eluent, to give **23** (2.4 g: 63% from **19**), which was recrystallized from methanol; mp 73.5—74.5 °C; $[\alpha]_D$ −9.6° (*c* 2.08); IR: 1722 $cm^{-1}$; $^1H$ NMR: 1.04 (3H, s, $C_{10}$–$CH_3$), 1.15 and 1.18 (each 3H and d, $J$=7 Hz, $-CH(C\underline{H}_3)_2$), 1.35 (3H, s, $C_4$–$CH_3$), 2.79 (1H, t, $J$=3 Hz, $C_{5\alpha}$–H), 3.21 (1H, m, $-C\underline{H}(CH_3)_2$), 3.60 (3H, s, $-CO_2CH_3$), 3.80 (3H, s, $-OCH_3$), 5.52 and 6.38 (each 1H and dd, $J$=10 and 3 Hz, $C_6$–H and $C_7$–H), 6.57 and 6.78 (each 1H and s, $C_{11}$–H and $C_{14}$–H). Found: C, 77.45; H, 9.08%. Calcd for $C_{22}H_{30}O_3$: C, 77.15; H, 8.83%.

*6,12-Dihydroxy-5βH-abieta-6,8,11,13-tetraen-18-oic Acid 18,6-Lactone (**24**).* Oxidation of **22** (45.7 g) in chloroform (340 ml) with a chloroform solution (270 ml) of perbenzoic acid (1.2 mol equivalent) was carried out, followed by refluxing with *p*-toluenesulfonic acid monohydrate (23.4 g) in toluene (1140 ml). This procedure, described for the preparation of **2**, yielded an unstable lactone (**24**) (40.0 g) as a solid. Aliquots of this were recrystallized from benzene; mp 163—165 °C; $[\alpha]_D$ −212° (*c* 0.660); IR: 3600, 3370br, 1794, 1690 $cm^{-1}$; $^1H$ NMR: 1.22 (6H, bd, $J$=7 Hz, $-CH(C\underline{H}_3)_2$), 1.47 (6H, s, $C_4$–$CH_3$ and $C_{10}$–$CH_3$), 2.62 (1H, d, $J$=3 Hz, $C_{5\beta}$–H), 3.10 (1H, m, $-C\underline{H}(CH_3)_2$), 5.22 (1H, bs, –OH; disappeared with $D_2O$), 5.93 (1H, d, $J$=3 Hz, $C_7$–H), 6.57 (1H, s, $C_{11}$–H), 6.71 (1H, s, $C_{14}$–H); UV: $\lambda_{max}^{EtOH}$ 286.5 nm (log ε 4.22). Found: C, 77.00; H, 7.68%. Calcd for $C_{20}H_{24}O_3$: C, 76.89; H, 7.74%.

*6-Hydroxy-12-methoxy-5βH-abieta-6,8,11,13-tetraen-18-oic Acid 18,6-Lactone (**25**).* *a)*: Oxidation of **23** (2.05 g) in chloroform with perbenzoic acid (1.1 mol equivalent), followed by treatment with *p*-toluenesulfonic acid monohydrate (1.14 g) in refluxing toluene, was carried out as described for the preparation of **2**. The crude product was purified by column chromatography on silica gel (70 g), using hexane–benzene (1:1) as the eluent, to afford **25** (1.12 g: 57%) as an oil; $[\alpha]_D$ −101° (*c* 3.40); IR: 1800, 1695 $cm^{-1}$; $^1H$ NMR: 1.18 (6H, bd, $J$=7 Hz, $-CH(C\underline{H}_3)_2$), 1.47 and 1.54 (each 3H and s, $C_4$–$CH_3$ and $C_{10}$–$CH_3$), 2.65 (1H, d, $J$=3 Hz, $C_{5\beta}$–H), 3.18 (1H, m, $-C\underline{H}(CH_3)_2$), 3.79 (3H, s, $-OCH_3$), 5.94 (1H, d, $J$=3 Hz, $C_7$–H), 6.66 (1H, s, $C_{11}$–H), 6.74 (1H, s, $C_{14}$–H). Found: C, 76.97; H, 8.06%. Calcd for $C_{21}H_{26}O_3$: C, 77.27; H, 8.03%.

*b)*: A stirred mixture of the crude **24** (2.44 g), dimethyl sulfate (1.05 ml), anhydrous potassium carbonate (10.8 g), and dry acetone (98 ml) was refluxed for 6 h. After the usual work-up, the crude product was chromatographed on silica gel (350 g), using hexane–benzene (2:3) as the eluent, to give an oil (0.48 g: 19% from **22**) whose IR and $^1H$ NMR spectra were identical with those of **25**. The compound **25** was so unstable that it converted into a complex mixture during the column chromatography.

*12-Acetoxy-6-hydroxy-5βH-abieta-6,8,11,13-tetraen-18-oic Acid 18,6-Lactone (**26**).* The above crude **24** (20.0 g) was acetylated with acetic anhydride (20 ml) in pyridine (60 ml). After the usual work-up, the product was chromatographed on silica gel (400 g), using benzene as the eluent, to give **26** (15.1 g: 69% from **22**) as an oil; $[\alpha]_D$ −70° (*c* 2.44); IR: 1800, 1758, 1694 $cm^{-1}$; $^1H$ NMR: 1.18 (6H, bd, $J$=7 Hz, $-CH(C\underline{H}_3)_2$), 1.45 and 1.50 (each 3H and s, $C_4$–$CH_3$ and $C_{10}$–$CH_3$), 2.22 (3H, s, $-OCOCH_3$), 2.67 (1H, d, $J$=3 Hz, $C_{5\beta}$–H), 2.89 (1H, m, $-C\underline{H}(CH_3)_2$), 5.98 (1H, d, $J$=3 Hz, $C_7$–H), 6.76 (1H, s, $C_{11}$–H), 6.84 (1H, s, $C_{14}$–H).

*6-Hydroxy-12-nitro-5βH-abieta-6,8,11,13-tetraen-18-oic Acid 18,6-Lactone (**27**).* A mixture of fuming nitric acid ($d$=1.50: 1.8 ml) and acetic anhydride (3.6 ml) was added dropwise to a stirred solution of **2** (6.0 g) in acetic anhydride (60 ml) at 0—5 °C over a period of 15 min. The mixture was stirred at room temperature for 1 h and then poured into ice–water. The aqueous mixture was stirred for another 30 min and then extracted with ether. The ether extract was washed successively with brine, aqueous sodium hydrogencarbonate, and brine. After being dried over sodium sulfate, the solvent was removed *in vacuo*. The residue was chromatographed on silica gel (350 g), using hexane–benzene (1:1) as the eluent, to give **27** (0.46 g: 7%), which was recrystallized from ethanol; mp 156.5—158 °C; $[\alpha]_D$ −29° (*c* 2.67); IR: 1808, 1690, 1515, 1345 $cm^{-1}$; $^1H$ NMR ($CDCl_3$): 1.27 and 1.29 (each 3H and d, $J$=7 Hz, $-CH(C\underline{H}_3)_2$), 1.55 and 1.62 (each 3H and s, $C_4$–$CH_3$ and $C_{10}$–$CH_3$), 2.81 (1H, d, $J$=3 Hz, $C_{5\beta}$–H), 3.48 (1H, m, $-C\underline{H}(CH_3)_2$), 6.15 (1H, d, $J$=3 Hz, $C_7$–H), 7.08 (1H, s, $C_{14}$–H), 7.69 (1H, s, $C_{11}$–H). Found: C, 70.20; H, 7.08; N, 4.07%. Calcd for $C_{20}H_{23}O_4N$: C, 70.36; H, 6.79; N, 4.10%.

*Reaction of **24** with Concentrated Sulfuric Acid in Acetic Acid.* A mixture of **24** (117 mg), concentrated sulfuric acid (0.61 ml), and acetic acid (5.85 ml) was refluxed for 1 h. After the same work-up as described for the preparation of **17**, the crude product was chromatographed on silica gel (12 g), using ether–benzene (5:95) as the eluent, to give an oil (6 mg: 4%) whose IR and $^1H$ NMR spectra were identical with those of (*R*)-6-acetoxy-3-(3-acetoxypropyl)-2,3-dihydro-7-isopropyl-3,4-dimethylnaphtho[2,3-*b*]furan-2-one (**29**).

Further elution gave (*R*)-3-(3-acetoxypropyl)-2,3-dihydro-6-hydroxy-7-isopropyl-3,4-dimethylnaphtho[2,3-*b*]furan-2-one (**28**) (32 mg: 23%) as an oil; $[\alpha]_D$ +25° (*c* 2.05); IR: 3600, 3320br, 1793, 1730 $cm^{-1}$; $^1H$ NMR: *ca.* 1.2 (2H, m, $-CH_2C\underline{H}_2CH_2OAc$), 1.30 (6H, d, $J$=7 Hz, $-CH(C\underline{H}_3)_2$), 1.57 (3H, s, $C_3$–$CH_3$), *ca.* 2.1 (2H, m, $-C\underline{H}_2CH_2CH_2OAc$), 1.94 (3H, s, $-OCOCH_3$), 2.48 (3H, s, $C_4$–$CH_3$), 3.32 (1H, m, $-C\underline{H}(CH_3)_2$), 3.86 (2H, t, $J$=6.5 Hz, $-CH_2CH_2C\underline{H}_2OAc$), 7.12 (2H, s, $C_5$–H and $C_9$–H; 11% NOE enhancement was observed on irradiation of the signal at δ 2.48), 7.43 (1H, s, $C_8$–H); UV: $\lambda_{max}^{EtOH}$ 238.5 nm (log ε 4.72), 268.5 (4.00), 279.5 (3.89), 290sh (3.61), 334.5 (3.49), 346.5 (3.57). Found: C, 71.04; H, 7.22%. Calcd for $C_{22}H_{26}O_5$: C, 71.33; H, 7.08%.

The compound **28** (25 mg) was acetylated with acetic anhydride (0.03 ml) in pyridine (0.05 ml) at room temperature for 1 h. After the usual work-up, the crude product was purified by column chromatography on silica gel to give **29** (21 mg); $[\alpha]_D$ +12° (*c* 2.09); IR: 1797, 1753, 1735 $cm^{-1}$; $^1H$ NMR: *ca.* 1.2 (2H, m, $-CH_2C\underline{H}_2CH_2OAc$), 1.29 (6H, d, $J$=7 Hz, $-CH(C\underline{H}_3)_2$), 1.60 (3H, s, $C_3$–$CH_3$), 1.91 (3H, s, $-OCOCH_3$), *ca.* 2.1 (2H, m, $-C\underline{H}_2CH_2CH_2OAc$), 2.32 (3H, s, $-OCOCH_3$), 3.05 (1H, m, $-C\underline{H}(CH_3)_2$), 3.83 (2H, t, $J$=6.5 Hz, $-CH_2CH_2C\underline{H}_2OAc$), 7.20 (1H, s, $C_9$–H), 7.49 (1H, s, $C_5$–H), 7.58 (1H, s, $C_8$–H). Found: C, 70.05; H, 6.98%. Calcd for $C_{24}H_{28}O_6$: C, 69.88; H, 6.84%.

*Reaction of **25** with Concentrated Sulfuric Acid in Acetic Acid.* A mixture of **25** (326 mg), concentrated sulfuric acid (1.48 ml), and acetic acid (16.5 ml) was refluxed for 1 h. After the same work-up as described for the preparation of **17**, the crude product was chromatographed on silica gel (30 g), using ether–benzene (1:99) as the eluent, to give (*R*)-3-(3-acetoxypropyl)-2,3-dihydro-7-isopropyl-6-methoxy-3,4-dimethylnaphtho[2,3-*b*]furan-2-one (**30**) as an oil (123 mg: 32%); $[\alpha]_D$ +25° (*c* 1.93); IR: 1800, 1740 $cm^{-1}$; $^1H$ NMR: *ca.* 1.2 (2H, m, $-CH_2C\underline{H}_2CH_2OAc$), 1.29 (6H, d, $J$=7 Hz, $-CH(C\underline{H}_3)_2$), 1.61 (3H, s, $C_3$–$CH_3$), 1.92 (3H, s, $-OCOCH_3$), *ca.* 2.1 (2H, m, $-C\underline{H}_2CH_2CH_2OAc$), 2.59 (3H,

s, $C_4$–$CH_3$), 3.38 (1H, m, –C<u>H</u>$(CH_3)_2$), 3.84 (2H, t, $J$=6.5 Hz, –$CH_2CH_2C\underline{H}_2OAc$), 3.95 (3H, s, –$OCH_3$), 7.07 (1H, s, $C_5$–H; 20% and 17% NOE enhancements were observed on irradiation of the signal at $\delta$ 2.59 and at $\delta$ 3.95 respectively), 7.18 (1H, s, $C_9$–H), 7.49 (1H, s, $C_8$–H). Found: C, 71.61; H, 7.35%. Calcd for $C_{23}H_{28}O_5$: C, 71.85; H, 7.34%.

*Reaction of* ***26*** *with Concentrated Sulfuric Acid in Acetic Acid.* A mixture of **26** (1.50 g), concentrated sulfuric acid (6.80 ml), and acetic acid (110 ml) was refluxed for 1.5 h. After the same work-up as described for the preparation of **17**, the crude product was immediately acetylated with acetic anhydride (1.5 ml) in pyridine (4.0 ml) at room temperature for 1 h. The crude acetate, after the usual work-up, was purified by column chromatography on silica gel (75 g), using ether–benzene (5:95) as the eluent, to afford an oil (0.73 g: 42%) whose IR and $^1$H NMR spectra were identical with those of **29**.

*Reaction of* ***27*** *with Concentrated Sulfuric Acid in Acetic Acid.* A mixture of **27** (132 mg), concentrated sulfuric acid (0.58 ml), and acetic acid (6.60 ml) was refluxed for 2 h. After the same work-up as described for the preparation of **17**, the crude product was chromatographed on silica gel (12 g), using hexane–benzene (2:3) as the eluent, to give the recovered **27** (85 mg: 64%).

Further elution with ether–benzene (3:97) afforded (*R*)-3-(3-acetoxypropyl)-2,3-dihydro-7-isopropyl-3,4-dimethyl-6-nitronaphtho[2,3-*b*]furan-2-one (**31**) (25 mg: 16%) as an oil; $[\alpha]_D$ +34° (*c* 0.955); IR: 1808, 1740, 1643, 1533, 1355 cm$^{-1}$; $^1$H NMR: *ca.* 1.25 (2H, m, –$CH_2C\underline{H}_2CH_2OAc$), 1.37 (6H, d, $J$=7 Hz, –$CH(C\underline{H}_3)_2$), 1.65 (3H, s, $C_3$–$CH_3$), 1.94 (3H, s, –$OCOCH_3$), *ca.* 2.15 (2H, m, –$C\underline{H}_2CH_2CH_2OAc$), 2.71 (3H, s, $C_4$–$CH_3$), 3.55 (1H, m, –C<u>H</u>$(CH_3)_2$), 3.87 (2H, t, $J$=6.5 Hz, –$CH_2CH_2C\underline{H}_2OAc$), 7.32 (1H, s, $C_9$–H), 7.74 (1H, s, $C_8$–H), 8.36 (1H, s, $C_5$–H; 20% NOE enhancement was observed on irradiation of the signal at $\delta$ 2.71); UV: $\lambda_{max}^{EtOH}$ 227 nm (log $\varepsilon$ 4.68), 261 (4.36), 278sh (4.18), 361 (3.96), 410sh (3.51), 430sh (3.40). Found: C, 66.03; H, 6.49; N, 3.40%. Calcd for $C_{22}H_{25}O_6N$: C, 66.15; H, 6.31; N, 3.51%.

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