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The Synthesis of Coleon B Tri-*O*-methyl Ether

Takashi MATSUMOTO,* Sachihiko IMAI, Katsumi NISHIZAKI, Fumio KURIHARA, and Fumitaka GOTO

Department of Chemistry, Faculty of Science, Hiroshima University, Higashisenda-machi, Naka-ku, Hiroshima 730

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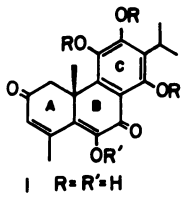
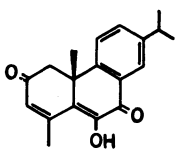
Methyl (+)-12-benzoyloxy-11,14-dioxo-8,12-abietadien-18-oate was converted into methyl 11,12,14-trimethoxy-8,11,13-abietatrien-18-oate (**8**). The Grignard reaction of **8** with phenylmagnesium bromide, followed by oxidation with lead tetraacetate, afforded 11,12,14-trimethoxy-19-norabieta-4(18),8,11,13-tetraene. This was then converted into 3α-bromo-11,12,14-trimethoxy-18-norabieta-8,11,13-trien-2-one (**15**) by a series of reactions: selenium dioxide oxidation, catalytic hydrogenation, dehydration, hydroxybromination, and Jones oxidation. Acetalization of **15** with 1,2-ethanediol, followed by oxidation with Jones reagent and then with oxygen in the presence of potassium *t*-butoxide, afforded 3-bromo-2,2-ethylenedioxy-6-hydroxy-11,12,14-trimethoxy-18-norabieta-5,8,11,13-tetraen-7-one, which was converted into (−)-coleon B tri-*O*-methyl ether (**4**) by hydrolysis and dehydrobromination. Another conversion of **15** into **4** was also achieved by a series of reactions: debromination, acetalization, Collins oxidation, oxygen oxidation, hydrolysis, and dehydrogenation.

Coleon B (**1**), a highly oxygenated tricyclic norditerpene phenol, has been isolated from the leaves of *Coleus igniarius* Schweinf. (Labiatae) by Eugster *et al.*[1] Recently, the synthesis of coleon B tetra-*O*-methyl ether (**2**) was reported by Burnell *et al.*[2] In the previous paper,[3] we also reported the synthesis of an A and B ring analog of coleon B, (−)-6-hydroxy-19-norabieta-3,5,8,11,13-pentaene-2,7-dione (**3**). As an extension of the previous work,[3] we here describe the successful synthesis of (−)-coleon B tri-*O*-methyl ether (**4**), starting from methyl (+)-12-benzoyloxy-11,14-dioxo-8,12-abietadien-18-oate (**5**)[4] which was prepared from (+)-dehydroabietic acid (**6**).



1 R=R'=H
2 R=R'=Me
4 R=Me, R'=H



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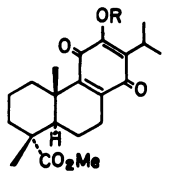
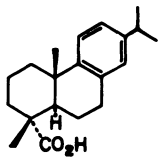


5 R=COPh



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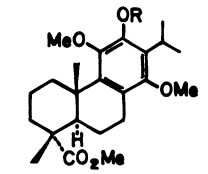
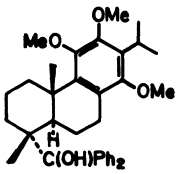
The 11,14-dioxo compound **5** was reduced with sodium dithionite in aqueous acetic acid at 80—95 °C or with zinc powder and dilute hydrochloric acid in benzene at 55—60 °C. The resulting phenol was methylated with methyl iodide in the presence of anhydrous potassium carbonate in refluxing ethyl methyl ketone to afford methyl 12-benzoyloxy-11,14-dimethoxy-8,11,13-abietatrien-18-oate (**7**) in 87.1% or 78.0% yield. The dimethoxy compound **7** was then converted into methyl 11,12,14-trimethoxy-8,11,13-abietatrien-18-oate (**8**: 82.4%) by alkaline hydrolysis and subsequent methylation. The Grignard reaction of **8** with phenylmagnesium bromide at 95—105 °C afforded a diphenylmethanol derivative (**9**: 71.3%). This was treated with lead tetraacetate and calcium carbonate in refluxing benzene to give 11,12,14-trimethoxy-19-norabieta-4(18),8,11,13-tetraene (**10**: 57.5%). The presence of an *exo*-methylene group at C-4 in **10** was supported by its ^{1}H NMR spectrum, which showed two broad singlet signals at δ 4.53 and 4.78 due to two olefinic protons. The tetraene **10** was oxidized with selenium dioxide in refluxing aqueous ethanol to yield 11,12,14-trimethoxy-19-norabieta-4(18),8,11,13-tetraen-3α-ol (**11**: 56.6%). The stereochemistry of the hydroxyl group at C-3 in **11** was assigned to be α-configuration from its ^{1}H NMR spectrum, which showed a broad signal due to the C-3 proton at δ 4.21 with half-height width of 5.4 Hz, suggesting the presence of an equatorial β proton. Catalytic hydrogenation of **11** in ethyl acetate over PtO_2 at room temperature afforded 11,12,14-trimethoxy-18-norabieta-8,11,13-trien-3α-ol[5] (**12**: 97.4%) which was dehydrated with phosphoryl chloride in refluxing pyridine to give 11,12,14-trimethoxy-18-norabieta-2,8,11,13-tetraene (**13**) in quantitative yield. The ^{1}H NMR spectrum of **13** showed doublet signals at δ 1.06 due to the C-4 methyl group and at δ 5.59 due to two olefinic protons. The tetraene **13** was treated with *N*-bromosuccinimide[6] in dimethyl sulfoxide containing a small quantity of water at room temperature under a stream of nitrogen to give a bromohydrin (**14**), which was used without purification in the next reaction. In the ^{1}H NMR spectrum of **14**, the down field shift of the signal (δ 1.38) due to the methyl group at C-10 relative to the corresponding signals for **12** (δ 1.28) and **13** (δ 1.26) suggested a 1,3-diaxial-*cis*-relationship between the methyl group and the new hydroxyl group. From the above spectral data and a well-documented mechanistic pathway (*trans*-diaxial addition),[7] the structure of **14** was assigned to be 3α-bromo-11,12,14-trimethoxy-18-norabieta-8,11,13-trien-2β-ol. Oxidation of the crude **14** in acetone with Jones reagent afforded 3α-bromo-11,12,14-trimethoxy-18-norabieta-8,11,13-trien-2-one (**15**) in 62.4% yield from **13**. To protect the carbonyl group as ethylene acetal, the

ketone **15** was refluxed with 1,2-ethanediol and *p*-toluenesulfonic acid in benzene to give a mixture of the C-3 epimeric acetals (**16**: 88.2%). Oxidation of the mixture (**16**) in acetone with Jones reagent afforded a mixture of the corresponding 7-oxo compounds (**17**: 81.8%[8]). This was then treated with oxygen in *t*-butyl alcohol in the presence of potassium *t*-butoxide to give a diosphenol derivative (**18**: 27.7%). The stereochemistry of the bromine atom at C-3 remains unsettled. Hydrolysis of **18** with dilute hydrochloric acid in refluxing acetic acid afforded a bromo ketone, which was immediately refluxed with pyridine to give the desired (−)-6-hydroxy-11,12,14-trimethoxy-19-norabieta-3,5,8,11,13-pentaene-2,7-dione (coleon B tri-*O*-methyl ether) (**4**) in 36.2% yield.



7 R=COPh
8 R=Me



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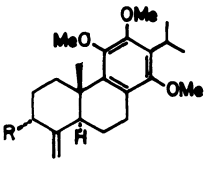
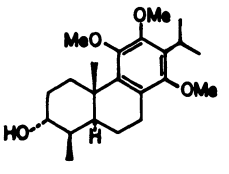


10 R=H
11 R=OH



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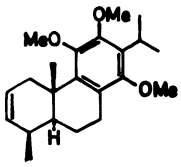

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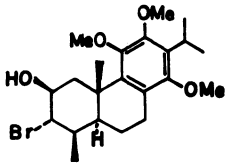

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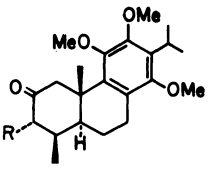
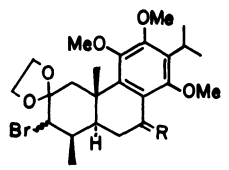
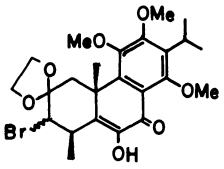


15 R=Br
19 R=H



16 R=H2
17 R=O



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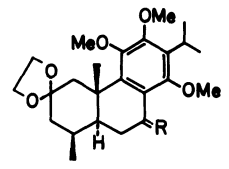
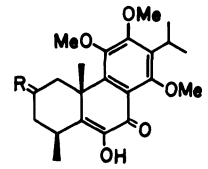
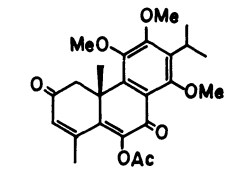


20 R=H2
21 R=O



22 R=OCH2CH2O
23 R=O



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Subsequently, another conversion of **15** into **4** was also carried out as follows. Debromination of **15** with sodium iodide and chlorotrimethylsilane in refluxing acetonitrile[9] afforded 11,12,14-trimethoxy-18-norabieta-8,11,13-trien-2-one (**19**: 90.0%). The ketone **19** was treated with 1,2-ethanediol and *p*-toluenesulfonic acid in refluxing benzene to give an acetal (**20**: 93.0%). Oxidation of **20** with Collins reagent[10] in dichloromethane at room temperature afforded the corresponding 7-oxo compound (**21**: 41.4%). This was further oxidized with oxygen in *t*-butyl alcohol in the presence of potassium *t*-butoxide to give a diosphenol derivative (**22**: 86.9%). Hydrolysis of **22** with dilute hydrochloric acid at room temperature afforded 6-hydroxy-11,12,14-trimethoxy-18-norabieta-5,8,11,13-tetraene-2,7-dione (**23**: 96.7%). Dehydrogenation of **23** with 2,3-dichloro-5,6-dicyano-*p*-benzoquinone and acetic acid in refluxing benzene under a stream of nitrogen produced **4** (*ca.* 59%).[8]

In the present study, the latter route for the synthesis of **4** from **15** was superior to the former one.

Experimental

All melting points are uncorrected. The IR spectra and optical rotations were measured in chloroform, and the ^{1}H NMR spectra in carbon tetrachloride at 60 MHz, with tetramethylsilane as an internal standard, unless otherwise stated; s: singlet, bs: broad singlet, d: doublet, bd: broad doublet, m: multiplet. The column chromatography was performed using Merck silica gel (0.063 mm).

Methyl 12-Benzoyloxy-11,14-dimethoxy-8,11,13-abietatrien-18-oate (7). a): A solution of sodium dithionite (11 g) in water (30 ml) was added dropwise at 80—95 °C to a stirred solution of methyl (+)-12-benzoyloxy-11,14-dioxo-8,12-abietadien-18-oate (**5**)[4] (550 mg) in acetic acid (30 ml). The mixture was stirred at this temperature for 15 min, cooled, and extracted with ether. The ether extract was washed successively with water, aqueous sodium hydrogencarbonate, and water. The solution was dried over sodium sulfate and evaporated *in vacuo* to give a crude phenol.

A stirred solution of the above crude phenol in ethyl methyl ketone (25 ml) was refluxed for 13 h with methyl iodide (3.0 ml) and anhydrous potassium carbonate (5.0 g). The mixture was cooled, diluted with water, and extracted with ether. The ether extract was washed successively with water, aqueous sodium thiosulfate, and water. The dried solution was evaporated *in vacuo*. The residue was recrystallized from methanol containing a small amount of acetone to give **7** (430 mg: 73.4%), mp 192.5—196 °C, $[\alpha]_D$+70.9°(*c* 1.27); IR: 1730, 1720 cm^{-1}; ^{1}H NMR: δ=3.53 and 3.60 (3H, each s, $-OCH_3$),[11] 3.66 (3H, s) and 3.73 (3H, s) ($-CO_2CH_3$ and $-OCH_3$), 7.43—7.7 (3H, m) and 8.08—8.3 (2H, m) ($-C_6H_5$). Found: C, 72.63; H, 7.85%. Calcd for $C_{30}H_{38}O_6$: C, 72.85; H, 7.74%. The mother liquor of recrystallization was evaporated *in vacuo*. The residue was chromatographed on silica gel (30 g), using ether–benzene (1:99) as the eluent, to give some additional **7** (80 mg after recrystallization: 13.7%).

b): A solution of **5** (5.080 g) in benzene (50 ml) was stirred at 55—60 °C for 30 min with a mixture of zinc powder (12 g) and dilute hydrochloric acid (10%:120 ml). After cooling, the benzene solution was separated. This was washed with water, dried over sodium sulfate, and evaporated *in vacuo* to give a

crude phenol. The crude phenol was immediately methylated for 14 h with methyl iodide (7.0 ml) and anhydrous potassium carbonate (25 g) in refluxing ethyl methyl ketone (70 ml). After the work-up as described in *a*), the crude product was purified by recrystallization and column chromatography to give **7** (4.174 g: 78.0%).

Methyl 11,12,14-Trimethoxy-8,11,13-abietatrien-18-oate (8). A mixture of **7** (14.482 g) and aqueous sodium hydroxide (10%: 72 ml) in ethanol (600 ml) was refluxed for 4 h. The mixture was concentrated *in vacuo*, acidified with dilute hydrochloric acid, and extracted with ether. The ether extract was washed successively with aqueous sodium hydrogencarbonate and brine, dried over sodium sulfate, and evaporated *in vacuo* to give a crude phenol.

A stirred solution of the above crude phenol in ethyl methyl ketone (150 ml) was refluxed for 16 h with methyl iodide (35 ml) and anhydrous potassium carbonate (50 g). The mixture was cooled, diluted with water, and extracted with ether. The ether extract was washed successively with aqueous sodium thiosulfate and brine, dried over sodium sulfate, and evaporated *in vacuo*. The residue was chromatographed on silica gel (800 g: 70—230 mesh), using ether—benzene (1:99) as the eluent, to give **8** (9.763 g: 82.4%). This was recrystallized from methanol, mp 96—97 °C, $[\alpha]_D$+97.4°(*c* 2.84), IR:1715 cm^{-1}; ^1H NMR:δ=1.25 (3H, s, C_4-CH_3), 1.30 (3H, s, C_{10}-CH_3), 1.30 (6H, d, J=7 Hz, -CH($C\underline{H}_3$)$_2$), 3.58, 3.62, 3.70, and 3.73 (each 3H and s, $-CO_2CH_3$ and 3-OCH_3). Found: C, 71.00; H, 9.06%. Calcd for $C_{24}H_{36}O_5$: C, 71.25; H, 8.97%.

Grignard Reaction of 8 with Phenylmagnesium Bromide. A solution of **8** (2.908 g) in dry ether (13 ml) was added to a refluxing ether solution of phenylmagnesium bromide prepared from magnesium turnings (0.699 g) and bromobenzene (3.0 ml) in dry ether (10 ml). The mixture was refluxed for 1 h and the ether was removed. The viscous residue was heated at 95—105 °C for 8 h. After cooling, the mass was carefully hydrolyzed with a mixture of dilute hydrochloric acid and ice, and then extracted with ether. The ether extract was washed successively with aqueous sodium thiosulfate and brine, dried over sodium sulfate, and evaporated *in vacuo*. The residue was chromatographed on silica gel (200 g: 70—230 mesh), using benzene as the eluent, to give a diphenylmethanol derivative **9** (2.710 g: 71.3%), $[\alpha]_D$ +89.8°(*c* 2.25), IR: 3587 cm^{-1}; ^1H NMR: δ=1.34 (6H, s, C_4-CH_3 and C_{10}-CH_3), 2.43 (1H, bs, -OH), 3.30 (3H, s) and 3.72 (6H, s) (3-OCH_3), 7.03—8.0 (10H, m, 2-C_6H_5). Found: C, 79.65; H, 8.57%. Calcd for $C_{35}H_{44}O_4$: C, 79.51; H, 8.39%.

11,12,14-Trimethoxy-19-norabieta-4(18),8,11,13-tetraene (10). A solution of **9** (166.3 mg) in dry benzene (2.0 ml) was added to a stirred suspension of lead tetraacetate (87%: 167.4 mg) and calcium carbonate (188.7 mg) in dry benzene (1.0 ml). The mixture was refluxed for 5 h, cooled, and then filtered. The filtrate was diluted with ether and the 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 (15 g), using hexane-benzene (7:3) as the eluent, to give **10** (62.3 mg: 57.5%), $[\alpha]_D$ +176°(*c* 3.15), IR: 1644 cm^{-1}; ^1H NMR: δ=1.10 (3H, s, C_{10}-CH_3), 1.30 (6H, d, J=7 Hz, -CH($C\underline{H}_3$)$_2$), 3.60 (3H, s) and 3.76 (6H, s) (3-OCH_3), 4.53 and 4.78 (each 1H and bs, -$\underline{C}$=CH_2). Found: C, 76.60; H, 9.64%. Calcd for $C_{22}H_{32}O_3$; C, 76.70; H, 9.36%.

11,12,14-Trimethoxy-19-norabieta-4(18),8,11,13-tetraen-3α-ol (11). Selenium dioxide (96%: 0.505 g) was added to a stirred solution of **10** (3.011 g) in ethanol (56.0 ml) and water (3.2 ml). The mixture was refluxed for 4 h, cooled, and then filtered. The filtrate was evaporated *in vacuo*. The residue was chromatographed on aluminium oxide (Merck activ. II—III: 180 g), using ether-benzene (2:8 and then 4:6) as the eluent, to give **11** (1.785 g: 56.6%). This was recrystallized from hexane, mp 141.5—142.5 °C, $[\alpha]_D$ +153° (*c* 1.91); IR: 3605, 3450 cm^{-1}; ^1H NMR: δ=1.05 (3H, s, C_{10}-CH_3), 1.30 (6H, d, J= 7 Hz, -CH($C\underline{H}_3$)$_2$), 1.63 (1H, s, -OH), 3.61 (3H, s) and 3.76 (6H, s) (3-OCH_3), 4.21 (1H, bs, $W_{1/2}$=5.4 Hz, $C_3\beta$-H), 4.62 and 4.97 (each 1H and bs, -$\underline{C}$=CH_2). Found: C, 73.26; H, 9.22%. Calcd for $C_{22}H_{32}O_4$: C, 73.30; H, 8.95%.

11,12,14-Trimethoxy-18-norabieta-8,11,13-trien-3α-ol (12). A solution of **11** (285 mg) in ethyl acetate (10.0 ml) was hydrogenated at room temperature for 3 h in an atmosphere of hydrogen using PtO_2 (60 mg). After the usual work-up, the crude product was chromatographed on silica gel (20 g), using ether-benzene (3:97) as the eluent, to give **12** (279 mg: 97.4%). This was recrystallized from acetone-hexane, mp 176—177 °C, $[\alpha]_D$ +103° (*c* 1.55); IR: 3613, 3462 cm^{-1}; ^1H NMR ($CDCl_3$): δ=1.01 (3H, d, J=7 Hz, C_4-CH_3), 1.28 (3H, s, C_{10}-CH_3), 1.33 (6H, d, J=7 Hz, -CH($C\underline{H}_3$)$_2$), 1.61 (1H, s, -OH), 3.65 (3H, s) and 3.80 (6H, s) (3-OCH_3). Found: C, 72.95; H, 9.71%. Calcd for $C_{22}H_{34}O_4$: C, 72.89; H, 9.45%.

11,12,14-Trimethoxy-18-norabieta-2,8,11,13-tetraene (13). A mixture of **12** (2.210 g), phosphoryl chloride (2.96 ml), and pyridine (28.0 ml) was refluxed for 1 h, cooled, and then poured into ice-dilute hydrochloric acid. The mixture was extracted with ether. The ether extract was washed with brine, dried over sodium sulfate, and evaporated *in vacuo*. The crude product was chromatographed on silica gel (110 g), using hexane-benzene (7:3) as the eluent, to give **13** (2.100 g: 100%), $[\alpha]_D$+292° (*c* 1.74), IR: 1646 cm^{-1}; ^1H NMR: δ=1.06 (3H, d, J=7.5 Hz, C_4-CH_3), 1.26 (3H, s, C_{10}-CH_3), 1.31 (6H, d, J=7 Hz, -CH($C\underline{H}_3$)$_2$), 3.59, 3.76, and 3.79 (each 3H and s, 3-OCH_3), 5.59 (2H, bd, J=3 Hz, C_2-H and C_3-H). Found: C, 76.96; H, 9.64%. Calcd for $C_{22}H_{32}O_3$: C, 76.70; H, 9.36%.

3α-Bromo-11,12,14-trimethoxy-18-norabieta-8,11,13-trien-2-one (15). A solution of **13** (1.076 g) in dimethyl sulfoxide (12.0 ml) containing a small quantity of water (0.17 ml) was stirred with *N*-bromosuccinimide (1.668 g) at room temperature for 2 h under a stream of nitrogen. The stirred mixture was cooled in an ice-water bath and aqueous sodium hydrogencarbonate was added. The mixture was extracted with ether. The ether extract was washed with brine, dried over sodium sulfate, and evaporated *in vacuo* to give the crude 3α-bromo-11,12,14-trimethoxy-18-norabieta-8,11,13-trien-2β-ol (**14**); IR: 3560, 3440 cm^{-1}; ^1H NMR: δ=1.31 (9H, d, J=7 Hz, C_4-CH_3 and -CH($C\underline{H}_3$)$_2$), 1.38 (3H, s, C_{10}-CH_3), 3.58, 3.74, and 3.83 (each 3H and s, 3-OCH_3).

The above crude bromohydrin (**14**) in acetone (12.0 ml) was oxidized with Jones reagent [2.5 M (1 M=1 mol dm^{-3}): 3.50 ml] at 0—5 °C for 5 min. The mixture was diluted with water and extracted with ether. The ether extract was washed with brine, dried over sodium sulfate, and evaporated *in vacuo*. The residue was chromatographed on silica gel (80 g), using benzene as the eluent, to give **15** (856 mg: 62.4%), $[\alpha]_D$ +153° (*c* 1.57), IR: 1706 cm^{-1}; ^1H NMR: δ= 1.06 (3H, d, J=7 Hz, C_4-CH_3), 1.26 (3H, s, C_{10}-CH_3), 1.31 (6H, d, J=7 Hz, -CH($C\underline{H}_3$)$_2$), 3.62, 3.74, and 3.82 (each 3H and s, 3-OCH_3), 4.06 (1H, bs, $C_3\beta$-H); MS (*m/z*): 440 (M^++2), 438 (M^+).

3-Bromo-2,2-ethylenedioxy-11,12,14-trimethoxy-18-norabieta-8, 11,13-triene (16). A mixture of **15** (405 mg), 1,2-ethanediol (1.14 ml), *p*-toluenesulfonic acid (200 mg), and dry benzene (20.0 ml) was refluxed for 8 h with a water separator containing 4 Å Molecular Sieves. The mixture was washed successively with aqueous sodium hydrogencarbonate and brine, dried over sodium sulfate, and evaporated *in vacuo*. The residue was chromatographed on silica gel (20 g), using hexane-benzene (2:8) as the eluent, to give a mixture of the C-3 epimers (**16**) (394 mg: 88.2%). MS (*m/z*): 484

(M^++2), 482 (M^+).

3-Bromo-2,2-ethylenedioxy-11,12,14-trimethoxy-18-norabieta-8,11,13-trien-7-one (17). A solution of **16** (109.0 mg) in acetone (3.0 ml) was oxidized with Jones reagent (2.5 M: 0.32 ml) at 0—10 °C for 35 min and then at room temperature for 1.5 h. The mixture was diluted with water and extracted with ether. The ether extract was washed with brine, dried over sodium sulfate, and evaporated *in vacuo*. The residue was chromatographed on silica gel (10 g), using hexane–benzene (1:9) as the eluent, to give the starting **16** (45.5 mg: 41.7%). Further elution with ether–benzene (5:95) gave **17** (53.5 mg: 47.7%, 81.8%[8]), IR: 1673 cm^{-1}; MS (*m/z*): 498 (M^++2), 496 (M^+).

3-Bromo-2,2-ethylenedioxy-6-hydroxy-11,12,14-trimethoxy-18-norabieta-5,8,11,13-tetraen-7-one (18). A stream of oxygen was bubbled in a stirred solution of **17** (171.5 mg) and potassium *t*-butoxide (433.2 mg) in *t*-butyl alcohol (8.0 ml) at 35 °C for 35 min. The mixture was diluted with water and extracted with ether. The ether extract was washed with brine, dried over sodium sulfate, and evaporated *in vacuo*. The residue was chromatographed on silica gel (10 g), using ether–benzene (1:99) as the eluent, to give **18** (48.9 mg: 27.7%). This was recrystallized from acetone–hexane, mp 173—174 °C, $[\alpha]_D$ +67.2° (*c* 0.625); IR: 3394, 1686, 1627 cm^{-1}; ^1H NMR (90 MHz): δ=1.33 (6H, d, *J*=7 Hz, $-CH(C\underline{H}_3)_2$), 1.49 (3H, d, *J*=7 Hz, C_4-CH_3), 1.63 (3H, s, $C_{10}-CH_3$), 2.10 (1H, d, *J*=14 Hz) and 2.80 (1H, d, *J*=14 Hz) (C_1-H_2), 3.73, 3.84, and 3.88 (each 3H and s, 3-OCH_3), 3.89—4.2 (4H, m, $-OCH_2-CH_2O-$), 4.33 (1H, d, *J*=11 Hz, C_3-H), 6.93 (1H, s, -OH). Found: C, 56.31; H, 6.18%. Calcd for $C_{24}H_{31}O_7Br$: C, 56.36; H, 6.11%.

6-Hydroxy-11,12,14-trimethoxy-19-norabieta-3,5,8,11,13-pentaene-2,7-dione (Coleon B Tri-O-methyl Ether) (4). A solution of **18** (13.9 mg) and dilute hydrochloric acid (10%: 0.1 ml) in acetic acid (2.0 ml) was refluxed for 1 h. The solution was concentrated *in vacuo*, diluted with water, and extracted with ether. The ether extract was successively washed with aqueous sodium hydrogencarbonate and brine, dried over sodium sulfate, and evaporated *in vacuo* to give a crude bromo ketone (11.0 mg), which was used without purification in the next reaction.

A solution of the above crude bromo ketone (11.0 mg) in pyridine (2.0 ml) was refluxed for 3 h. The solution was cooled, poured into dilute hydrochloric acid, and extracted with ether. The ether extract was washed successively with aqueous sodium thiosulfate and brine, dried over sodium sulfate, and evaporated *in vacuo*. The residue was chromatographed on silica gel (5.0 g), using ether–benzene (1:99) as the eluent, to give **4** (3.8 mg: 36.2%), $[\alpha]_D$ −52.8° (*c* 0.625); IR: 3325, 1651, 1626 cm^{-1}; ^1H NMR (90 MHz): δ=1.35 (6H, d, *J*=6.5 Hz, $-CH(C\underline{H}_3)_2$), 1.63 (3H, s, $C_{10}-CH_3$), 2.47 (3H, d, *J*=2 Hz, C_4-CH_3), 2.23 (1H, d, *J*=16 Hz) and 3.62 (1H, d, *J*=16 Hz) (C_1-H_2), 3.74, 3.89, and 3.93 (each 3H and s, 3-OCH_3), 5.98 (1H, bs, C_3-H), 7.89 (1H, s, -OH); MS (*m/z*): 386 (M^+).

11,12,14-Trimethoxy-18-norabieta-8,11,13-trien-2-one (19). A mixture of **15** (308.6 mg) and sodium iodide (316.0 mg) in acetonitrile (5.0 ml) was stirred at room temperature for 5 min. A solution of chlorotrimethylsilane (98%: 0.27 ml) in acetonitrile (5.0 ml) was then added to the above mixture, and this was refluxed for 2 h. The mixture was cooled, diluted with water, and extracted with ether. The ether extract was washed successively with aqueous sodium thiosulfate and brine, dried over sodium sulfate,and evaporated *in vacuo*. The residue was chromatographed on silica gel (20 g), using ether–benzene (3:97) as the eluent, to give **19** (228.7 mg: 90.0%). This was recrystallized from hexane, mp 111.5—112.5 °C, $[\alpha]_D$ +111° (*c* 0.820) (lit,[1] mp 111.5—113°C, $[\alpha]_D$ +98°), IR: 1697 cm^{-1}; ^1H NMR: δ=1.07 (3H, d, *J*=7 Hz, C_4-CH_3), 1.29 (3H, s, $C_{10}-CH_3$), 1.30 (6H, d, *J*=7 Hz, $-CH(C\underline{H}_3)_2$), 3.60, 3.74, and 3.81 (each 3H and s, 3-OCH_3). Found: C, 73.05; H, 8.94%. Calcd for $C_{22}H_{32}O_4$: C, 73.30; H, 8.95%.

2,2-Ethylenedioxy-11,12,14-trimethoxy-18-norabieta-8,11,13-triene (20). A mixture of **19** (55.2 mg), 1,2-ethanediol (0.2 ml), and *p*-toluenesulfonic acid (60 mg) in dry benzene (10.0 ml) was refluxed for 16 h with a water separator containing 4 Å Molecular Sieves. After the work-up as described for the preparation of **16**, the crude product was chromatographed on silica gel (10 g), using ether–benzene (1:99) as the eluent, to give **20** (57.6 mg: 93.0%). This was recrystallized from hexane, mp 123—125.5 °C, $[\alpha]_D$ +70.6° (*c* 1.105); ^1H NMR: δ=1.11 (3H, d, *J*=7 Hz, C_4-CH_3), 1.30 (6H, d, *J*=7 Hz, $-CH(C\underline{H}_3)_2$), 1.37 (3H, s, $C_{10}-CH_3$), 3.58, 3.75, and 3.78 (each 3H and s, 3-OCH_3), 3.75—4.0 (4H, m, overlap,$-OCH_2-CH_2O-$). Found: C, 71.05; H, 8.78%. Calcd for $C_{24}H_{36}O_5$: C, 71.25; H, 8.97%.

2,2-Ethylenedioxy-11,12-14-trimethoxy-18-norabieta-8,11,13-trien-7-one (21). Chromium trioxide (700 mg) was added to a stirred solution of **20** (122.5 mg) and pyridine (1.13 ml) in dichloromethane (7.0 ml). The mixture was stirred at room temperature for 23 h, diluted with water, and extracted with ether. The ether extract was washed successively with aqueous sodium hydroxide, water, dilute hydrochloric acid, and brine. The dried solution was evaporated *in vacuo*. The residue was chromatographed on silica gel (10 g), using ether–benzene (5:95) as the eluent, to give **21** (52.5 mg: 41.4%). This was recrystallized from acetone–hexane, mp 151.5—152.5 °C, $[\alpha]_D$ +145° (*c* 0.415), IR: 1670 cm^{-1}; ^1H NMR: δ=1.28 (6H, d, *J*=7 Hz, $-CH(C\underline{H}_3)_2$), 1.44 (3H, s, $C_{10}-CH_3$), 3.66 (3H, s),and 3.80 (6H, s) (3-OCH_3). Found: C, 68.57; H, 8.43%. Calcd for $C_{24}H_{34}O_6$: C, 68.87; H, 8.19%.

2,2-Ethylenedioxy-6-hydroxy-11,12,14-trimethoxy-18-norabieta-5,8,11,13-tetraen-7-one (22). A stream of oxygen was bubbled in a stirred solution of **21** (22.2 mg) and potassium *t*-butoxide (66.6 mg) in *t*-butyl alcohol (3.5 ml) at 35—40 °C for 100 min. After the work-up as described for the preparation of **18**, the crude product was chromatographed on silica gel (10 g), using ether–benzene (5:95) as the eluent, to give **22** (18.4 mg: 86.9%). This was recrystallized from acetone–hexane, mp 216—217 °C, $[\alpha]_D$ +40.0°(*c* 0.475); IR: 3394, 1684, 1625 cm^{-1}; ^1H NMR (90 MHz): δ=1.32, 1.34, and 1.36 (each 3H, d, and *J*=7 Hz, C_4-CH_3 and $-CH(C\underline{H}_3)_2$), 1.65 (3H, s, $C_{10}-CH_3$), 1.81 (1H, d, *J*=14 Hz) and 2.90 (1H, d, *J*=14 Hz) (C_1-H_2), 3.72, 3.86, and 3.88 (each 3H and s, 3-OCH_3), 6.92 (1H, s, -OH); MS (*m/z*): 432 (M^+).

6-Hydroxy-11,12,14-trimethoxy-18-norabieta-5,8,11,13-tetraene-2,7-dione (23). A solution of **22** (33.5 mg) and dilute hydrochloric acid (10%: 0.75 ml) in tetrahydrofuran (3.0 ml) was stirred at room temperature for 20 h. The solution was diluted with ether. The ether solution was washed with brine, dried over sodium sulfate, and evaporated *in vacuo*. The residue was chromatographed on silica gel (10 g), using ether–benzene (5:95) as the eluent, to give **23** (29.1 mg: 96.7%). This was recrystallized from acetone–hexane, mp 169—170 °C, $[\alpha]_D$ +61.5° (*c* 0.390); IR: 3397, 1705, 1628 cm^{-1}; ^1H NMR (90 MHz): δ=1.34 (6H, d, *J*=7 Hz, $-CH(C\underline{H}_3)_2$), 1.44 (3H, d, *J*=7 Hz, C_4-CH_3), 1.72 (3H, s, $C_{10}-CH_3$), 2.20 (1H, d, *J*=16 Hz) and 3.57 (1H, d, *J*=16 Hz) (C_1-H_2), 3.72, 3.86, and 3.90 (each 3H and s, 3-OCH_3), 7.06 (1H, s, -OH); MS (*m/z*): 388 (M^+).

Dehydrogenation of 23. A stirred mixture of **23** (10.0 mg), 2,3-dichloro-5,6-dicyano-*p*-benzoquinone (98%: 6.5 mg), and acetic acid (0.15 ml) in dry benzene (3.0 ml) was refluxed for 37 h under a stream of nitrogen. The mixture was cooled and then filtered. The filtrate was washed successively with sodium hydrogencarbonate and brine, dried over sodium sulfate, and evaporated *in vacuo*. The residue

was chromatographed on silica gel (10 g), using ether–benzene (5:95) as the eluent, to give the starting **23** (2.2 mg: 22%). Further elution gave a mixture (5.3 mg) of **4** and **23**. The ^{1}H NMR spectrum of the mixture indicated that it was composed of approximately 3.5 mg (35%, 59%[8]) of **4** and 1.8 mg (18%) of **23**.

The above mixture of **4** and **23** was acetylated at 80—85 °C for 1 h with acetic anhydride (0.2 ml) in pyridine (0.4 ml). After the usual work-up, the crude product was chromatographed on silica gel (10 g), using ether–benzene (1:9) as the eluent, to give 6-acetoxy-11,12,14-trimethoxy-19-norabieta-3,5,8,11,13-pentaene-2,7-dione (**24**) (3.3 mg). IR: 1765, 1655 cm^{-1}; ^{1}H NMR (90 MHz): δ=1.32 (6H, d, J=7 Hz, -CH(CH_3)$_2$), 1.68 (3H, s, C_{10}–CH_3), 2.31 (3H, d, J=1.8 Hz, C_4–CH_3), 2.32 (3H, s, -OCOCH_3), 3.68, 3.84, and 3.92 (each 3H and s, 3-OCH_3), 6.06 (1H, bs, C_3-H); MS (m/z): 428 (M^+).

Hydrolysis of **24** with dilute hydrochloric acid in refluxing ethanol afforded **4**.

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