Synthesis of A and B Rings Analog of Coleon B

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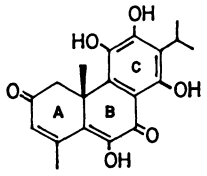
Catalytic hydrogenation of 19-norabieta-4(18),8,11,13-tetraen-3α-ol over Raney Ni and subsequent dehydration afforded 18-norabieta-2,8,11,13-tetraene, which was converted into 3α-bromo-18-norabieta-8,11,13-trien-2-one (**8**) *via* a bromohydrin. Acetalization of **8** with 1,2-ethanediol in the presence of *p*-toluenesulfonic acid afforded a mixture of 3α-bromo-2,2-ethylenedioxy-18-norabieta-8,11,13-triene (**10**) and its 3β-bromo isomer (**11**) in a ratio of *ca.* 2 : 3. Oxidation of **10** and **11** with chromium trioxide in acetic acid gave the corresponding ketones **12** and **13**. The ketone **13** was then converted into a diosphenol derivative, 3β-bromo-2,2-ethylenedioxy-6-hydroxy-18-norabieta-5,8,11,13-tetraen-7-one (**14**), by treatment with oxygen in the presence of potassium *t*-butoxide. Hydrolysis of **14** with dilute hydrochloric acid followed by dehydrobromination afforded the desired analog, 6-hydroxy-19-norabieta-3,5,8,11,13-pentaene-2,7-dione. A related A/B ring oxygenated compound, 19-norabieta-3,5,8,11,13-pentaene-2,7-dione was also synthesized from **12** and **13** *via* the corresponding 6α-bromo derivatives.

Coleon B (**1**) is a rare tricyclic norditerpene phenol isolated from *Coleus iguiarius* Schweinf. (Labiatae) by Eugster *et al.*[1] To establish the synthetic route of this highly-oxygenated norditerpene, we investigated the oxidation of rings A/B of dehydroabietic acid (**2**); the introduction of oxygen functions at the C-11, C-12, and C-14 positions in ring C has already been achieved in our laboratory.[2] This paper will describe the synthesis of A and B rings analog (**3**) of coleon B, starting from 19-norabieta-4(18),8,11,13-tetraen-3α-ol (**4**) which was prepared from **2** by the known procedure.[3-5]



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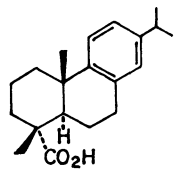

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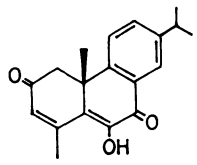

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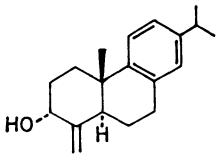

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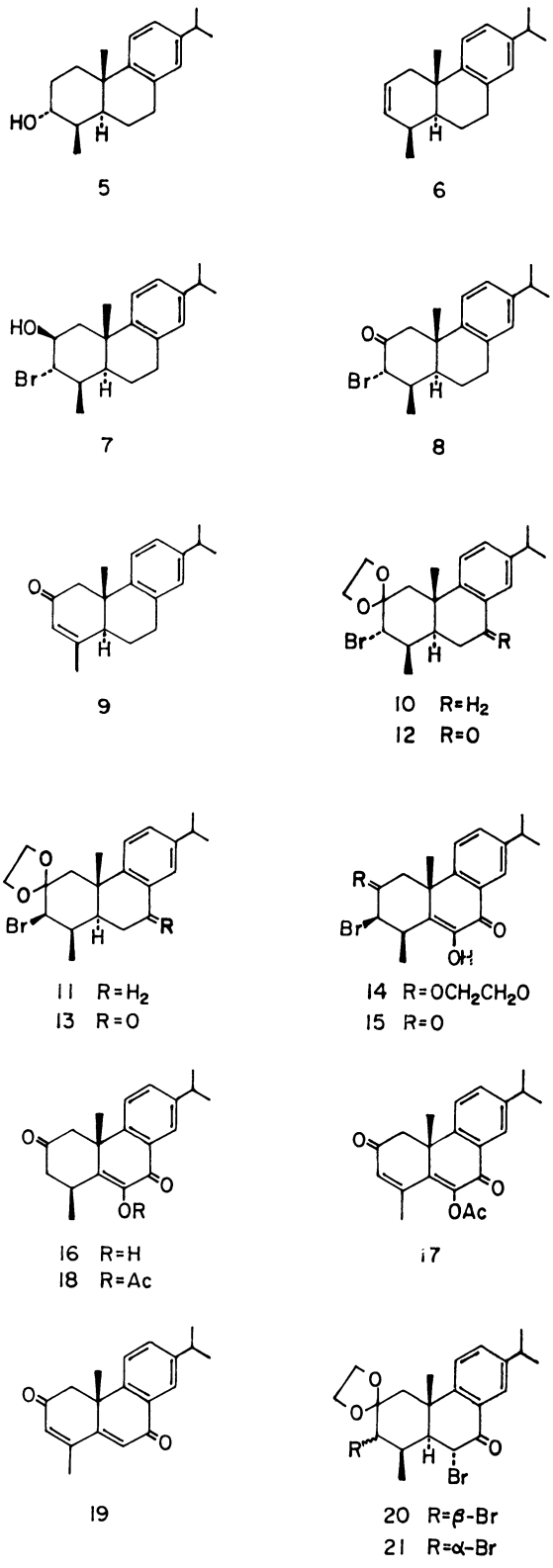
Catalytic hydrogenation of **4** in ethanol over Raney Ni at room temperature afforded 18-norabieta-8,11,13-trien-3α-ol (**5**),[6,7] which was dehydrated with phosphoryl chloride in refluxing pyridine to give 18-norabieta-2,8,11,13-tetraene (**6**) in 65.3% yield from **4**. The ^{1}H NMR spectrum of **6** showed doublet signals at δ 1.05 due to the C-4 methyl group and at δ 5.66 due to the two vinylic protons. The tetraene **6** was treated with *N*-bromosuccinimide in dimethyl sulfoxide containing a small quantity of water at 20—25 °C under a stream of nitrogen to give a bromohydrin (**7**) which, without purification, was used in the next reaction. The structure of **7** as indicated was predicted by a well-documented mechanistic pathway[8] and was substantiated spectroscopically. In the ^{1}H NMR spectrum of **7**, the downfield shift of the signal (δ 1.36) due to the methyl group at the C-10 position relative to the corresponding signal (δ 1.20) for **6** suggested a 1,3-diaxial-*cis*-relationship between the methyl goup and the new hydroxyl group. Consequently, the structure of **7** was assigned to be 3α-bromo-18-norabieta-8,11,13-trien-2β-ol. Oxidation of the crude **7** in acetone with Jones reagent at 0 °C afforded 3α-bromo-18-norabieta-8,11,13-trien-2-one (**8**) in 69.1% yield from **6**. This bromo ketone **8** was easily dehydrobrominated by heating at 120—125 °C with lithium carbonate and lithium bromide in *N*,*N*-dimethylformamide under a stream of nitrogen; an α,β-unsaturated ketone, 19-norabieta-3,8,11,13-tetraen-2-one (**9**), was obtained. The structure of **9** was supported by its IR (1654, 1622 cm^{-1}) and ^{1}H NMR (δ 1.99, C_4–CH_3; 5.86, C_3–H) spectra. From the formation of **9**, the position of the bromine atom in **7** and **8** was conclusively assigned to be the C-3 position. To protect the carbonyl group as ethylene acetal, the ketone **8** was refluxed with 1,2-ethanediol and *p*-toluenesulfonic acid in benzene to give two epimeric acetals in 81.1%yield, **10** and **11**, in a ratio of *ca.* 2 : 3. Hydrolysis of **10** with dilute hydrochloric acid in refluxing acetic acid afforded the original ketone **8**, which was also obtained by the same hydrolysis of **11**. The ^{1}H NMR spectrum of **10** showed a multiplet signal at δ *ca.* 3.8—4.3 due to the ethylenedioxy group at the C-2 position, while that of **11** showed the corresponding signal at δ 3.98 as a broad singlet with half-height width of 6 Hz. These spectral data suggested[9] the presence of an axial bromine atom in **10** and an equatorial one in **11**. Thus, the structures of **10** and **11** were determined respectively to be 3α-bromo-2,2-ethylenedioxy-18-norabieta-8,11,13-triene and 3β-bromo-2,2-ethylenedioxy-18-norabieta-8,11,13-triene. The acetals **10** and **11** were then oxidized with chromium trioxide in acetic acid to give the corresponding 7-oxo compounds, **12** and **13** in yields of 52.6 and 52.2% respectively. Treatment of **13** in *t*-butyl alcohol with oxygen in the presence of potassium *t*-butoxide afforded a diosphenol derivative, 3β-bromo-2,2-ethylenedioxy-6-hydroxy-18-norabieta-5,8,11,13-tetraen-7-one (**14**), in 61.0% yield. The IR spectrum of **14** showed bands at 3432, 1663, 1638, and 1608 cm^{-1} corresponding to a diosphenol moiety. The compound **14** was hydrolyzed with dilute hydrochloric acid in refluxing acetic acid and the resulting

ketone (**15**), without purification, was treated at 120—125 °C with lithium carbonate and lithium bromide in *N,N*-dimethylformamide under a stream of nitrogen to give the desired 6-hydroxy-19-norabieta-3,5,8,11,13-pentaene-2,7-dione (**3**) together with a small amount of 6-hydroxy-18-norabieta-5,8,11,13-tetraene-2,7-dione (**16**). Acetylation of **3** and **16** with acetic anhydride in pyridine afforded the corresponding monoacetates, **17** and **18**. These acetates were easily hydrolyzed with dilute hydrochloric acid in refluxing ethanol to give the original diones, **3** and **16**.

Subsequently, the synthesis of 19-norabieta-3,5,8,11,-13-pentaene-2,7-dione (**19**) was carried out as follows. The ketone **13** was brominated with pyridinium tribromide in dichloromethane at room temperature to give 3β,6α-dibromo-2,2-ethylenedioxy-18-norabieta-8,11,13-trien-7-one (**20**) in 76.5% yield. The stereochemistry of the C-6 position in **20** was supported by its ^{1}H NMR spectrum, which showed a doublet signal due to the C-6 proton at δ 4.84 with coupling constant of 13 Hz, suggesting the presence of an axial β proton. Hydrolysis of **20** with dilute hydrochloric acid in refluxing acetic acid afforded the corresponding 2,7-dioxo compound which, without purification, was converted into **19** in 93.0% yield by treatment with lithium carbonate and lithium bromide in *N,N*-dimethylformamide at 120—125 °C. Similarly, the ketone **12** was also converted into **19** *via* the corresponding 6α-bromo compound (**21**).



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 60 MHz, with tetramethylsilane as an internal standard, unless otherwise stated. The chemical shifts are presented in terms of δ values; s: singlet, bs: broad singlet, d: doublet, bd: broad doublet, dd: double doublet, m: multiplet. The column chromatography was performed using Merck silica gel.

18-Norabieta-8,11,13-trien-3α-ol (5). A solution of **4**[3-5] (418 mg) in ethanol (10 ml) was hydrogenated at room temperature for *ca.* 3 h in an atmosphere of hydrogen using Raney Ni (W-7) prepared from nickel–aluminium alloy (50%: 1.078 g). After the usual work-up, the crude product was recrystallized from hexane to give **5**[6,7] as colorless crystals (305 mg: 72.3%), mp 117—121 °C. Further crystallization gave an analytical sample; mp 122—123 °C; $[\alpha]_D$ +76.0°; IR: 3616, 3412 cm^{-1}; ^{1}H NMR: 0.92 (3H, d, J=7.5 Hz, C_4–CH_3), 1.11 (3H, s, C_{10}–CH_3), 1.22 (6H, d, J=7 Hz, –CH(CH_3)$_2$), 1.93 (1H, s, –OH), 3.68 (1H, bs, $W_{1/2}$=5.5 Hz, C_3–H), 6.65—7.15 (3H, m, aromatic protons). Found: C, 83.83; H, 10.60%. Calcd for $C_{19}H_{28}O$: C, 83.77; H, 10.36%.

18-Norabieta-2,8,11,13-tetraene (6). A mixture of **5** (504 mg), phosphoryl chloride (0.9 ml), and pyridine (4.0 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 purified by column chromatography on silica gel (30 g), using hexane as the eluent, to give **6** (425 mg: 90.3%) as an oil; $[\alpha]_D$ +291°; ^{1}H NMR: 1.05 (3H, d, J=7.5 Hz, C_4–CH_3), 1.20 (3H, s, C_{10}–CH_3), 1.22 (6H, d, J=7 Hz, –CH(CH_3)$_2$), 5.66 (2H, d, J=3 Hz, C_2–H and C_3–H), 6.70—7.20 (3H, m, aromatic protons). Found: C, 89.91; H, 10.58%. Calcd for $C_{19}H_{26}$: C, 89.70; H, 10.30%.

3α-Bromo-18-norabieta-8,11,13-trien-2-one (8). A solution of **6** (425 mg) in dimethyl sulfoxide (7.0 ml) containing a small quantity of water (0.1 ml) was stirred with *N*-bromosuccinimide (620 mg) at 20—25 °C for 1 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-18-norabieta-8,11,13-trien-2β-ol (**7**) (596 mg) as an oil; IR: 3570, 3370 cm^{-1}; ^1H NMR: 1.22 (6H, d, J=7 Hz, $-CH(C\underline{H}_3)_2$), 1.29 (3H, d, J=7.5 Hz, C_4-CH_3), 1.36 (3H, s, $C_{10}-CH_3$).

The crude **7** (596 mg) in acetone (7.0 ml) was oxidized with Jones reagent [2.5 M (1 M=1 mol dm^{-3}): 1.2 ml] at 0 °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 (35 g), using hexane–benzene (1 : 1) as the eluent, to give **8** (403 mg: 69.1%) as an oil which responded positively to the Beilstein halogen test; $[\alpha]_D$ +185°; IR: 1707 cm^{-1}; ^1H NMR: 1.16 (3H, d, J=7.5 Hz, C_4-CH_3), 1.17 (3H, s, $C_{10}-CH_3$), 1.22 (6H, d, J=7 Hz, $-CH(C\underline{H}_3)_2$), 4.06 (1H, bs, C_3–H), 6.83 (1H, bs) and 6.97 (2H, s) (aromatic protons). Found: C, 65.03; H, 7.33%. Calcd for $C_{19}H_{25}OBr$: C, 65.33; H, 7.23%.

*19-Norabieta-3,8,11,13-tetraen-2-one (**9**).* A mixture of **8** (44 mg), lithium carbonate (30 mg), and lithium bromide (38 mg) in *N,N*-dimethylformamide (2.0 ml) was stirred at 120—125 °C for 3 h in a stream of nitrogen. The reaction mixture was cooled, poured into dilute hydrochloric acid, and extracted with ether. The ether extract was washed with aqueous sodium thiosulfate and brine, dried over sodium sulfate, and evaporated *in vacuo*. The residue was purified by column chromatography on silica gel (10 g), using ether–benzene (3 : 97) as the eluent, to give **9** (32 mg; 92.3%) as an oil; $[\alpha]_D$ +121°; IR: 1654, 1622 cm^{-1}; ^1H NMR: 1.12 (3H, s, $C_{10}-CH_3$), 1.23 (6H, d, J=7 Hz, $-CH(C\underline{H}_3)_2$), 1.99 (3H, bs, C_4-CH_3), 5.86 (1H, bs, C_3–H), 6.70—7.20 (3H, m, aromatic protons). Found: C, 84.72; H, 9.30%. Calcd for $C_{19}H_{24}O$: C, 85.02; H, 9.01%.

*Acetalization of the Bromo Ketone **8**.* A mixture of **8** (833 mg), 1,2-ethanediol (3.0 ml), *p*-toluenesulfonic acid (784 mg), and dry benzene (20 ml) was refluxed for 10 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 crude product was chromatographed on silica gel (30 g), using hexane–benzene (65 : 35) as the eluent, to give 3α-bromo-2,2-ethylenedioxy-18-norabieta-8,-11,13-triene (**10**) (311 mg: 33.1%). It was recrystallized from ether–methanol, mp 114.5—115.5 °C, $[\alpha]_D$ +8.7°; ^1H NMR: 1.20 (6H, d, J=7 Hz, $-CH(C\underline{H}_3)_2$), 1.26 (3H, d, J=7.5 Hz, C_4-CH_3), 1.31 (3H, s, $C_{10}-CH_3$), 1.70 and 2.48 (each 1H and d, J=14 Hz, C_1–H_2), 3.80—4.50 (5H, m, $-OCH_2CH_2O-$ and C_3–H), 6.74 (1H, s) and 6.91 (2H, bs) (aromatic protons). Found: C, 64.23; H, 7.32%. Calcd for $C_{21}H_{29}O_2Br$: C, 64.12; H, 7.45%.

Further elution with the same solvent gave 3β-bromo-2,2-ethylenedioxy-18-norabieta-8,11,13-triene (**11**) (451 mg: 48.0%) as an oil; $[\alpha]_D$ +108°; ^1H NMR: 1.22 (9H, d, J=7 Hz, $-CH(C\underline{H}_3)_2$ and C_4-CH_3), 1.30 (3H, s, $C_{10}-CH_3$), 3.98 (4H, bs, $-OCH_2CH_2O-$), 4.09 (1H, d, J=3 Hz, C_3–H), 6.77 (1H, s), and 6.93 (2H, bs) (aromatic protons). Found: C, 64.40; H, 7.47%. Calcd for $C_{21}H_{29}O_2Br$: C, 64.12; H, 7.45%.

*Hydrolysis of the Acetals **10** and **11**.* *a)*: A mixture of **10** (190 mg) and dilute hydrochloric acid (10%: 0.7 ml) in acetic acid (6.0 ml) was refluxed for 1 h, concentrated *in vacuo*, 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 (10 g), using hexane–benzene (1 : 1) as the eluent, to give an oil (129 mg: 76.3%), whose IR and ^1H NMR spectra were identical with those of **8**.

b): A mixture of **11** (70 mg) and dilute hydrochloric acid (10%: 0.4 ml) in acetic acid (2.0 ml) was refluxed for 1 h. After the same work-up as described in *a*), the crude product was chromatographed on silica gel (10 g), using hexane–benzene (6 : 4) as the eluent, to give an oil (41 mg: 66.5%), whose IR and ^1H NMR spectra were identical with those of **8**.

*3α-Bromo-2,2-ethylenedioxy-18-norabieta-8,11,13-trien-7-one (**12**).* A stirred solution of **10** (625 mg) in acetic acid (7.0 ml) was oxidized with chromium trioxide (614 mg) at room temperature for 2.5 h. The mixture 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*. The residue was chromatographed on silica gel (40 g), using ether–benzene (1 : 99) as the eluent, to give **12** (340 mg: 52.6%). It was recrystallized from methanol; mp 136.5—139 °C; $[\alpha]_D$ −16.5°; IR: 1676, 1607 cm^{-1}; ^1H NMR: 1.25 (6H, d, J=7 Hz, $-CH(C\underline{H}_3)_2$), 1.33 (3H, d, J=7.5 Hz, C_4-CH_3), 1.41 (3H, s, $C_{10}-CH_3$), 3.85—4.50 (5H, m, $-OCH_2CH_2O-$ and C_3–H), 7.09 (1H, d, J=8 Hz, C_{11}–H), 7.29 (1H, dd, J=2 and 8 Hz, C_{12}–H), 7.78 (1H, d, J=2 Hz, C_{14}–H). Found: C, 61.97; H, 6.70%. Calcd for $C_{21}H_{27}O_3Br$: C, 61.92; H, 6.69%.

*3β-Bromo-2,2-ethylenedioxy-18-norabieta-8,11,13-trien-7-one (**13**).* A stirred solution of **11** (2.542 g) in acetic acid (14 ml) was oxidized with chromium trioxide (2.525 g) as described for the preparation of **12**. The crude product was chromatographed on silica gel (100 g), using ether–benzene (1 : 99) as the eluent, to give **13** (1.374 g: 52.2%). It was recrystallized from methanol; mp 141—142 °C; $[\alpha]_D$ +65.2°; IR: 1673, 1608 cm^{-1}; ^1H NMR: 1.27 (6H, d, J=7 Hz, $-CH(C\underline{H}_3)_2$), 1.30 (3H, d, J=7.5 Hz, C_4-CH_3), 1.39 (3H, s, $C_{10}-CH_3$), 3.90—4.20 (5H, m, $-OCH_2CH_2O-$ and C_3–H), 7.14 (1H, d, J=8 Hz, C_{11}–H), 7.34 (1H, dd, J=2 and 8 Hz, C_{12}–H), 7.81 (1H, d, J=2 Hz, C_{14}–H). Found: C, 61.63; H, 6.44%. Calcd for $C_{21}H_{27}O_3Br$: C, 61.92; H, 6.69%.

*3β-Bromo-2,2-ethylenedioxy-6-hydroxy-18-norabieta-5,8,11,13-tetraen-7-one (**14**).* A stream of oxygen was bubbled in a stirred solution of **13** (1.226 g) and potassium *t*-butoxide (3.80 g) in *t*-butyl alcohol (25 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 (30 g), using benzene as the eluent, to give **14** (772 mg: 61.0%). It was recrystallized from methanol; mp 180—181 °C; $[\alpha]_D$ +17.2°; IR: 3432, 1663, 1638, 1608 cm^{-1}; ^1H NMR: 1.30 (6H, d, J=7 Hz, $-CH(C\underline{H}_3)_2$), 1.51 (3H, d, J=7.5 Hz, C_4-CH_3), 1.61 (3H, s, $C_{10}-CH_3$), 2.37 (2H, s, C_1–H_2), 3.40—4.40 (5H, m, $-OCH_2CH_2O-$ and C_3–H), 6.67 (1H, s, –OH), 7.31 (2H, bs, C_{11}–H and C_{12}–H), 7.95 (1H, bs, C_{14}–H). Found: C, 59.98; H, 6.18%. Calcd for $C_{21}H_{25}O_4Br$: C, 60.01; H, 6.01%.

*3β-Bromo-6-hydroxy-18-norabieta-5,8,11,13-tetraene-2,7-dione (**15**).* A mixture of **14** (684 mg) and dilute hydrochloric acid (10%: 2.5 ml) in acetic acid (15 ml) was refluxed for 70 min, concentrated *in vacuo*, diluted with water, and then 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 the crude **15** (670 mg) which, without purification, was used in the next reaction.

*Dehydrobromination of the 2,7-Dione **15**.* A mixture of the crude **15** (670 mg), lithium carbonate (380 mg), and lithium bromide (450 mg) in *N,N*-dimethylformamide (8.0 ml) was stirred at 120—125 °C for 3 h in a stream of nitrogen. After the same work-up as described for the preparation of **9**, the

crude product was purified by column chromatography on silica gel (40 g), using ether–benzene (0.5 : 99.5) as the eluent, to give 6-hydroxy-18-norabieta-5,8,11,13-tetraene-2,7-dione (**16**) (63 mg). It was recrystallized from ether–hexane; mp 95—96.5 °C; $[\alpha]_D$ +18.8°; IR: 3428, 1708, 1661, 1638, 1608 cm^{-1}; ^1H NMR: 1.32 (6H, d, J=7 Hz, $-CH(C\underline{H}_3)_2$), 1.43 (3H, d, J=7.5 Hz, C_4–CH_3), 1.59 (3H, s, C_{10}–CH_3), 6.87 (1H, s, -OH), 7.40 (2H, d, J=2 Hz, C_{11}–H and C_{12}–H), 7.98 (1H, bs, C_{14}–H). Found: C, 76.72; H, 7.65%. Calcd for $C_{19}H_{22}O_3$: C, 76.48; H, 7.43%.

Subsequent elution gave a mixture of **16** and 6-hydroxy-19-norabieta-3,5,8,11,13-pentaene-2,7-dione (**3**) (188 mg), whose purification is described later.

Further elution gave **3** (83 mg); $[\alpha]_D$ −215°; IR: 3365, 1664, 1646, 1611 cm^{-1}; ^1H NMR: 1.33 (6H, d, J=7 Hz, $-CH(C\underline{H}_3)_2$), 1.54 (3H, s, C_{10}–CH_3), 2.32 and 2.99 (each 1H and d, J=15 Hz, C_1–H_2), 2.49 (3H, d, J=2 Hz, C_4–CH_3), 5.98 (1H, bs, C_3–H), 7.48 (2H, d, J=2 Hz, C_{11}–H and C_{12}–H), 7.63 (1H, s, -OH), 8.02 (1H, bs, C_{14}–H). Found: C, 76.72; H, 6.97%. Calcd for $C_{19}H_{20}O_3$: C, 77.00; H, 6.80%.

The above mixture of **16** and **3** (188 mg) was acetylated with acetic anhydride (1.0 ml) and pyridine (2.0 ml) at 80—85 °C for 1 h. After the usual work-up, the crude product was chromatographed on silica gel (15 g), using ether–benzene (2 : 98) as the eluent, to give 6-acetoxy-19-norabieta-3,5,8,-11,13-pentane-2,7-dione (**17**) (139 mg); $[\alpha]_D$ −95.9°; IR: 1771, 1662, 1613 cm^{-1}; ^1H NMR: 1.30 (6H, d, J=7 Hz, $-CH(C\underline{H}_3)_2$), 1.61 (3H, s, C_{10}–CH_3), 2.34 (6H, s, C_4–CH_3 and $-OCOCH_3$), 6.05 (1H, bs, C_3–H), 7.41 (2H, d, J=2 Hz, C_{11}–H and C_{12}–H), 7.96 (1H, bs, C_{14}–H). Found: C, 74.23; H, 6.60%. Calcd for $C_{21}H_{22}O_4$: C, 74.53; H, 6.55%.

Further elution with ether–benzene (7 : 93) gave 6-acetoxy-18-norabieta-5,8,11,13-tetraene-2,7-dione (**18**) (34 mg): IR: 1766, 1715, 1663, 1612 cm^{-1}; ^1H NMR: 1.29 (6H, d, J=7 Hz, $-CH(C\underline{H}_3)_2$), 1.35 (3H, d, J=7.5 Hz, C_4–CH_3), 1.63 (3H, s, C_{10}–CH_3), 2.32 (3H, s, $-OCOCH_3$), 7.37 (2H, bs, C_{11}–H and C_{12}–H), 7.93 (1H, bs, C_{14}–H).

*Hydrolysis of the Acetates **17** and **18**.* *a)*: A mixture of **17** (143 mg) and dilute hydrochloric acid (10%: 2.0 ml) in ethanol (7.0 ml) was refluxed for 2.5 h, concentrated *in vacuo*, diluted with water, and then 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 (12 g), using ether–benzene (3 : 97) as the eluent, to give an oil (114 mg), whose IR and ^1H NMR spectra were identical with those of **3**.

b): A mixture of **18** (33 mg) and dilute hydrochloric acid (10%: 1.0 ml) in ethanol (5.0 ml) was refluxed for 1.5 h. After the same work-up as described in *a*), the crude product was purified by column chromatography on silica gel (5.0 g), using ether–benzene (2 : 98) as the eluent, to give **16** (23 mg), whose IR and ^1H NMR spectra were identical with those of the authentic sample.

*3β,6α-Dibromo-2,2-ethylenedioxy-18-norabieta-8,11,13-trien-7-one (**20**).* A mixture of **13** (611 mg) and pyridinium tribromide (80%: 1190 mg) in dichloromethane (14 ml) was stirred at room temperature for 160 min. The mixture was diluted with water and extracted with ether. The ether extract was washed successively with aqueous sodium thiosulfate, dilute hydrochloric acid, and brine, dried over sodium sulfate, and evaporated *in vacuo*. The residue was purified by column chromatography on silica gel (60 g), using benzene as the eluent, to give **20** (558 mg: 76.5%) as an oil; $[\alpha]_D$ +84.8°; IR: 1687, 1607 cm^{-1}; ^1H NMR: 1.27 (6H, d, J=7 Hz, $-CH(C\underline{H}_3)_2$), 1.36 (3H, d, J=7.5 Hz, C_4–CH_3), 1.39 (3H, s, C_{10}–CH_3), 2.10 (1H, bd, J=14 Hz) and 2.62 (1H, d, J=14 Hz) (C_1–H_2), 3.90—4.30 (5H, m, $-OCH_2CH_2O-$ and C_3–H), 4.84 (1H, d, J=13 Hz, C_6–H), 7.14 (1H, d, J=8 Hz, C_{11}–H), 7.35 (1H, dd, J=2 and 8 Hz, C_{12}–H), 7.80 (1H, d, J=2 Hz, C_{14}–H). Found: C, 51.78; H, 5.55%. Calcd for $C_{21}H_{26}O_3Br_2$: C, 51.87; H, 5.61%.

*3α,6α-Dibromo-2,2-ethylenedioxy-18-norabieta-8,11,13-trien-7-one (**21**).* A mixture of **12** (262 mg) and pyridinium tribromide (80%: 410 mg) in dichloromethane (6.0 ml) was stirred at room temperature for 160 min. After the same work-up as described for the preparation of **20**, the crude product was chromatographed on silica gel (30 g), using benzene as the eluent, to give **21** (222 mg: 70.9%) as a solid; $[\alpha]_D$ +30.7°; IR: 1685, 1608 cm^{-1}; ^1H NMR ($CDCl_3$): 1.27 (6H, d, J=7 Hz, $-CH(C\underline{H}_3)_2$), 1.40 (3H, d, J=7.5 Hz, C_4–CH_3), 1.43 (3H, s, C_{10}–CH_3), 1.98 and 2.60 (each 1H and d, J=14 Hz, C_1–H_2), 3.95—4.55 (5H, m, $-OCH_2CH_2O-$ and C_3–H), 5.02 (1H, d, J=13 Hz, C_6–H), 7.17 (1H, d, J=8 Hz, C_{11}–H), 7.44 (1H, dd, J=2 and 8 Hz, C_{12}–H), 7.90 (1H, d, J=2 Hz, C_{14}–H).

*19-Norabieta-3,5,8,11,13-pentaene-2,7-dione (**19**).* *a)*: A mixture of **20** (486 mg) and dilute hydrochloric acid (10%: 1.2 ml) in acetic acid (8.0 ml) was refluxed for 1 h, concentrated *in vacuo*, diluted with water, and then 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 the crude 2,7-dioxo compound (395 mg) which, without purification ,was used in the next reaction.

A mixture of the crude 2,7-dioxo compound (395 mg), lithium carbonate (391 mg), and lithium bromide (480 mg) in *N,N*-dimethylformamide (6.5 ml) was stirred at 120—125 °C for 3 h in a stream of nitrogen. After the same work-up as described for the preparation of **9**, the crude product was purified by column chromatography on silica gel (15 g), using ether–benzene (3 : 97) as the eluent, to give **19** (261 mg: 93.0%) as an oil; $[\alpha]_D$ −51.2°; IR: 1668, 1650, 1608 cm^{-1}; ^1H NMR: 1.32 (6H, d, J=7 Hz, $-CH(C\underline{H}_3)_2$), 1.51 (3H, s, C_{10}–CH_3), 2.29 (3H, d, J=2 Hz, C_4–CH_3), 6.13 (1H, bs, C_3–H), 6.63 (1H, s, C_6–H), 7.43 (2H, d, J=2 Hz, C_{11}–H and C_{12}–H), 7.94 (1H, bs, C_{14}–H). Found: C, 81.09; H, 7.32%. Calcd for $C_{19}H_{20}O_2$: C, 81.39; H, 7.19%.

b): A mixture of **21** (209 mg) and dilute hydrochloric acid (10%: 0.6 ml) in acetic acid (4.0 ml) was refluxed for 1 h, concentrated *in vacuo*, diluted with water, and then extracted with ether. The ether extract was washed successively with aqueous sodium hydrogencarbonate and brine, dried over sodium sulfate, and evaporated *in vacuo*.

The crude 2,7-dioxo compound (179 mg), without purification, was stirred at 120—125 °C for 3 h with lithium carbonate (180 mg), lithium bromide (220 mg), and *N,N*-dimethylformamide (3.0 ml) in a stream of nitrogen. The reaction mixture was treated as described for the preparation of **9** and then purified by column chromatography on silica gel (15 g), using ether–benzene (2 : 98) as the eluent. The IR and ^1H NMR spectra of the product (96 mg: 79.8%) were identical with those of **19**.

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