C-Aromatic Steroids. Synthesis of 11,17ξ-Dimethoxy-18-norandrosta-4,8,11,13-tetraen-3-one

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Birch reduction of 5-hydroxy-7-methoxy-1*H*-cyclopenta[*a*]naphthalen-3(2*H*)-one (1) afforded 3,5-dihydroxy-7-methoxy-2,3,6,9-tetrahydro-1*H*-cyclopenta[*a*]naphthalene (2a) in high yield. The latter has been transformed into the title *C*-aromatic steroid (7a) through steps involving methylation, hydrolysis, *C*-methylation, and Robinson annulation. The analogous synthesis of 11,17ξ-dimethoxygona-4,8,11,13-tetraen-3-one (7b) is also described.

CYCLOPENTANAPHTHALENES, which are readily accessible by the general synthetic route developed by Robinson,[1] offer themselves as attractive intermediates for 11-oxygenated-18-norsteroids because of the favourable pattern of substitution present. Bateman and Robinson[2] reported that catalytic hydrogenation of 5-acetoxy-7-methoxy-1*H*-cyclopenta[*a*]naphthalen-3(2*H*)-one gave two main products, in both of which the 3-oxygen function had been eliminated. Previous attempts[3,4] to reduce the terminal ring of these tricyclics by the Birch method led to mixtures of products, because, in the compounds so reduced, either or both the rings of the naphthalene system underwent reduction, and further, the benzylic oxygen function in the five-membered ring was susceptible to elimination.

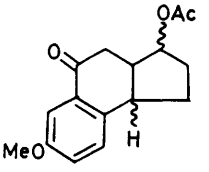
RESULTS AND DISCUSSION

In the present synthesis the above side-reactions could be effectively suppressed through the judicious choice of an appropriate derivative, namely, 5-hydroxy-7-methoxycyclo-1*H*-penta[*a*]naphthalen-3(2*H*)-one (1) as the substrate in the crucial metal–ammonia reduction. This was based on the work of Birch and Subba Rao[6] who carried out the lithium–ammonia reduction of the tetracyclic analogue of (1), namely, 5-hydroxy-8-methoxy-1*H*-cyclopenta[*a*]phenanthren-3(2H)-one, to obtain a product in which the hydroxy-substituted ring was not reduced and the 3-oxygen function was not eliminated. The known cyclopentanaphthol (1) is easily prepared from *p*-methoxyacetophenone and furfural in five steps by the Robinson sequence.[2] With lithium–ammonia–tetrahydrofuran (1) underwent the anticipated selective reduction of the terminal ring, accompanied by the reduction of the carbonyl function, smoothly to afford 3,5-dihydroxy-7-methoxy-2,3,6,9-tetrahydro-1*H*-cyclopenta[*a*]naphthalene(2a) in high yield, ranging from 80 to 85%. The Δ^7-structure assigned to (2a) is based on its n.m.r. spectrum, in which the triplet for the vinyl proton is clearly seen.

Enol ethers (2c) and (2d) were readily hydrolysed in acidic solutions to the corresponding cyclopenta-β-tetralone derivatives (3c) and (3d) respectively. These are referred to as β-tetralones for brevity in what follows.

Following this procedure with the total product mixture from the Birch reduction of (1), other tetralones were isolated as by-products.

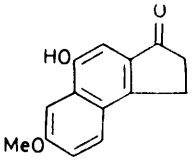
The crude Birch reduction product from (1) was



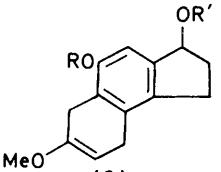
(4)

acetylated with acetic anhydride–pyridine. Hydrolysis of the enol ethers occurred during the usual work-up, and chromatography of the mixture on silica gel afforded (3d), along with a less polar minor product to which the most plausible α-tetralone structure (4) is assigned on the basis of its i.r. and n.m.r. spectra. The aromatic carbonyl structure was confirmed by the typical crimson 2,4-dinitrophenylhydrazone derivative. However, the stereochemistry of the C/D ring junction and that of the 3-acetoxy-group remain undetermined.

Methylation of (2a) was best carried out stepwise. Treatment with methyl iodide–potassium carbonate in acetone gave (2b), which was further methylated by means of methyl iodide–silver oxide–chloroform to give (2c). The latter was smoothly hydrolysed with methanolic hydrochloric acid to the β-tetralone (3c). When the total Birch reduction product was subjected to the same sequence of reactions, (3c) was isolated along with a small

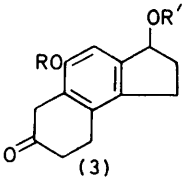


(1)



(2)

a; R = R′ = H c; R = R′ = Me
b; R = Me, R′ = H d; R = R′ = Ac



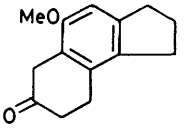
(3)

a; R = R′ = H d; R = R′ = Ac
b; R = Me, R′ = H e; R = Me, R′ = Et
c; R = R′ = Me

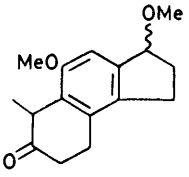
quantity of the known [4] deoxygenated by-product (5). The two readily separated on a silica gel column

It is interesting to note that when (2c) was treated with ethanolic hydrochloric acid, it was converted into the 3-ethoxy-β-tetralone (3e). Furthermore, (2b) gave with methanolic hydrochloric acid or oxalic acid the β-tetralone (3c). In subsequent runs (3c) was conveniently prepared by this procedure.

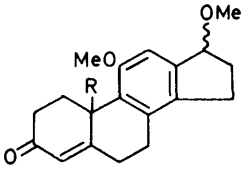
The dimethoxycyclopentatetralone (3c) was methylated readily by means of methyl iodide and sodium methoxide in methanol, and the required 6-methyl derivative (6) was isolated in satisfactory yield. It gave



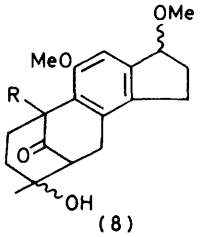
(5)



(6)



(7)
a ; R = Me
b ; R = H



(8)
a ; R = Me
b ; R = H

a single spot on t.l.c. and the clean n.m.r. spectrum indicated that it was one of the diastereoisomers in nearly pure state.

The annulation reaction on (6) was carried out using methyl vinyl ketone and sodium methoxide in methanol. Two products were formed and these were easily separated by chromatography on silica gel. The normal Robinson annulation product, which happened to be the minor one, was characterized as 11,17ξ-dimethoxy-18-norandrosta-4,8,11,13-tetraen-3-one (7a). The major product was the keto-alcohol (8a) identified on the basis of analysis and spectral data. It was found to be resistant to dehydration or rearrangement when treated with moderately strong acids. However when (8a) was heated with 10% potassium hydroxide it was transformed into the desired enone (7a) obviously through a retro-aldol reaction followed by aldol condensation and dehydration. Similar observations have been recorded by previous workers.[5] The cyclopenta-β-tetralone (3c) likewise underwent the annulation reaction under similar conditions to afford, as in the previous case, the two enone (7b) and the keto-alcohol (8b), in the ratio *ca.* 1 : 2. Although further work would be needed to completely elucidate the stereochemistry of the products (7a), (7b), (8a), and (8b) it may be noted that each reaction described here afforded a diastereoisomer which, after purification, appeared clearly homogeneous.

EXPERIMENTAL

Melting points are uncorrected. I.r. spectra were recorded on a Perkin-Elmer 257-B; u.v. spectra on a Perkin-Elmer 137; and n.m.r. spectra on a Varian XL-100A. Silica gel (100—200 mesh), activated by heating at 110 °C for 6 h, was used for column chromatography.

5-Hydroxy-7-methoxy-1H-cyclopenta[a]naphthalen-3(2H)-one (1).—Compound (1) was prepared from 4-methoxyacetophenone and furfural in five steps following the procedure of Bateman and Robinson,[2] m.p. 255—257 °C (lit.,[2] 250—255 °C); $\nu_{max.}$ (Nujol) 3 150br, 1 675 (CO), 1 655 (H-bonded CO), 1 615, and 1 590 cm^{-1}; $\nu_{max.}$ ($CHCl_3$) 3 150, 1 695 (CO), 1 655w, and 1 605 cm^{-1}.

3,5-Dihydroxy-7-methoxy-2,3,6,9-tetrahydro-1H-cyclopenta[a]naphthalene (2a).—Phenol (1) (11.4 g) in tetrahydrofuran (1.2 l) was added to liquid ammonia (2.5 l) in a three-necked 5-l flask placed under the hood. Lithium metal (2.5 g) was added in small pieces with stirring. The ammonia solution remained blue for a short time after which the colour disappeared. The mixture was stirred for 2 h after which ammonium chloride (100 g) was added. Ammonia was allowed to evaporate, and tetrahydrofuran was distilled off. On addition of ice–water, *3,5-dihydroxy-7-methoxy-2,3,6,9-tetrahydro-1H-cyclopenta[a]naphthalene* (2a) separated as a solid (11.4 g), crystallized from methanol, m.p. 181—183 °C (average yield in several runs 80—85%) (Found: C, 72.45; H, 7.1. $C_{14}H_{16}O_3$ requires C, 72.34; H, 6.94%); $\nu_{max.}$ (Nujol) 3 450 (OH), 3 300, 1 675 (enol ether alkene), and 1 595 (aromatic) cm^{-1}; δ(DMSO–$CDCl_3$) 3.6 (3 H, s, OMe), 4.60 (1 H, d, *J* 6 Hz, D_2O-exchangeable, 3-OH), 4.74 (1 H, t, *J* 2 Hz, vinyl), 4.98 (1 H, m, *J* 1 Hz; 3-H), 6.7 (1 H, s, aromatic), and 8.66 (1 H, s, D_2O-exchangeable, 5-OH).

3,5-Diacetoxy-7-methoxy-2,3,6,9-tetrahydro-1H-cyclopenta[a]naphthalene (2d).—The crude Birch reduction product of phenol (1) (0.2 g) was dissolved in dry pyridine (10 ml) and acetic anhydride (1 ml), and left at 0—5 °C overnight. Pyridine and acetic anhydride were removed by vacuum-distillation, and the residue was extracted with benzene, washed with water, and dried over sodium sulphate. Removal of the solvent gave the *diacetyl derivative* (2d), crystallized from benzene–hexane (0.170 g), m.p. 108 °C (Found: C, 68.45; H, 6.55. $C_{18}H_{20}O_5$ requires C, 68.34; H, 6.37%); $\nu_{max.}$ (Nujol) 1 760 (aromatic acetate), 1 740 (3-acetate), 1 685 (enol ether alkene), and 1 595 (aromatic) cm^{-1}; δ($CDCl_3$) 2.06 (3 H, s, 3-OAc), 2.32 (3 H, s, 5-OAc), 2.06—2.98 (4 H, ring CH_2), 3.22—3.38 (4 H, ring CH_2), 3.64 (3 H, s, 7-OMe), 4.78 (1 H, t, *J* 3 Hz, vinyl), 6.14 (1 H, q, *J* 4 Hz, 3-H), and 6.98 (1 H, s, aromatic).

3,5-Diacetoxy-8,9-dihydro-1H-cyclopenta[a]naphthalen-7(6H)-one (3d).—The crude Birch reduction product of phenol (1) (2.5 g) was dissolved in dry pyridine (30 ml) and acetic anhydride (2.5 ml) and left overnight at 0—5 °C. The reaction mixture was taken up in ether and the solution washed with dilute hydrochloric acid and brine. The extracted compound was dissolved in ethanol (25 ml) and dilute hydrochloric acid (3 ml) was added. Hydrolysis to the β-tetralone appeared complete, as shown by t.l.c. The product obtained after ether extraction (2.3 g) was chromatographed on a silica gel column (50 g). The first fraction, eluted with 10% ethyl acetate–hexane, was obtained as a pale brown oil (0.22 g). It is assigned the structure 3-acetoxy-7-methoxy-2,3,3a,9b-tetra-1*H*-hydrocyclopenta-[*a*]naphthalen-5(4*H*)-one (4) on the basis of the following

spectral data; $\nu_{max.}$ (thin film) 1 735 (ester CO), 1 680 (aromatic CO), 1 605, and 1 500 (aromatic) cm^{-1}; $\delta(CDCl_3)$ 2.06 (3 H, s, 3-OAc), 3.84 (3 H, s, 6-OMe), 4.9 (1 H, m, 3-H), and 7.12—7.42 (3 H, m, aromatic). It gave a crimson 2,4-*dinitrophenylhydrazone*, m.p. 188 °C (Found: N, 12.56. $C_{22}H_{22}N_4O_7$ requires N, 12.33%).

The major product, 3,5-*diacetoxy*-8,9-*dihydro*-1H-*cyclopenta*[a]*naphthalen*-7(6H)-*one* (3d) (1.53 g), was eluted with 20% ethyl acetate–hexane. It crystallized from ethyl acetate–hexane as colourless plates, m.p. 103—104 °C (Found: C, 67.25; H, 6.1. $C_{17}H_{18}O_5$ requires C, 67.54; H, 6.00%); $\nu_{max.}$ (Nujol) 1 755 (aromatic acetate CO), 1 735 (3-acetate CO), 1 715 (CO), and 1 600 (aromatic) cm^{-1}; $\delta(CDCl_3)$ 2.08 (3 H, s, 3-OAc), 2.32 (3 H, s, 5-OAc), 2.08—3.10 (8 H, ring CH_2), 3.40 (2 H, s, 6-CH_2), 6.22 (1 H, q, *J* 4 Hz, 3-H), and 7.04 (1 H, aromatic). It gave a yellow 2,4-dinitrophenylhydrazone, m.p. 134—135 °C.

3-*Hydroxy*-5,7-*dimethoxy*-2,3,6,9-*tetrahydro*-1H-*cyclopenta*[a]*naphthalene* (2b).—The mixture of the crude product (1.5 g) from Birch reduction of (1), acetone (200 ml), methyl iodide (5 ml), and potassium carbonate (10 g) was stirred for 28 h at room temperature and the progress of the reaction monitored by t.l.c. Acetone was distilled off and the residue extracted with ether. The usual work-up gave the enol ether (2b) (1.6 g). It crystallized from benzene–hexane, m.p. 127—129 °C (lit.,[3] 127—128 °C) (Found: C, 73.45; H, 7.2. Calc. for $C_{15}H_{18}O_3$: C, 73.15; H, 7.37%).

3,5,7-*Trimethoxy*-2,3,6,9-*tetrahydro*-1H-*cyclopenta*[a]*naphthalene* (2c).—The enol ether (2b) (0.76 g), chloroform (25 ml), silver oxide (1.19 g), and methyl iodide (0.6 ml) were mixed and stirred for 20 h at room temperature. More methyl iodide (0.4 ml) was added during this period in small amounts. After filtration, chloroform was distilled off. The residue gave, on crystallization from benzene–hexane, the *enol ether* (2c) (0.560 g), m.p. 87—89 °C (Found: C, 74.0; H, 7.55. $C_{16}H_{20}O_3$ requires C, 73.82; H, 7.74%); $\nu_{max.}$ (Nujol) 1 685 (enol ether alkene) and 1 600 (aromatic) cm^{-1}; $\delta(CDCl_3)$ 2.02—3.02 (4 H, ring CH_2), 3.32 (4 H, ring CH_2), 3.42 (3 H, s, 3-OMe), 3.62 (3 H, s, 7-OMe), 3.84 (3 H, s, 5-OMe), 4.78 (2 H, m; vinyl and 3-H), and 6.76 (1 H, s; aromatic).

3-*Ethoxy*-5-*methoxy*-8,9-*dihydro*-1H-*cyclopenta*[a]*naphthalen*-7(6H)-*one* (3e).—To the enol ether (2c) (0.4 g) dissolved in ethanol (25 ml), dilute hydrochloric acid (2 ml) was added. After 0.5 h the reaction mixture was poured into water and extracted with ether. The extract (0.43 g) was mounted on a silica gel column (15 g). Elution with 10% ethyl acetate–hexane afforded almost pure 3-*ethoxy*-5-*methoxy*-8,9-*dihydro*-1H-*cyclopenta*[a]*naphthalen*-7(6H)-*one* (3e). It crystallized from ethyl acetate–hexane (0.210 g), m.p. 78—79 °C (Found C, 73.3; H, 7.5. $C_{16}H_{20}O_3$ requires C, 73.82; H, 7.74%); $\nu_{max.}$ (Nujol) 1 720 (CO) and 1 600 (aromatic) cm^{-1}; $\delta(CDCl_3)$ 1.24 (3 H, t, *J* 7 Hz, OCH_2Me), 2.02—3.04 (8 H, methylene protons), 3.42—3.72 (2 H, q, *J* 7 Hz, OCH_2Me), 3.50 (2 H, s, 6-CH_2), 3.84 (3 H, s, 5-OMe), 4.92 (1 H, t, *J* 6 Hz, 3-H), and 6.82 (1 H, s, aromatic).

3,5-*Dimethoxy*-8,9-*dihydro*-1H-*cyclopenta*[a]*naphthalen*-7(6H)-*one* (3c).—*Procedure A*. A mixture of enol ether (2c) (0.695 g), methanol (20 ml), and dilute hydrochloric acid (2 ml) was left at room temperature for 0.5 h, then diluted with water and extracted with ether. The extract was subjected to chromatography on a silica gel column (30 g). Elution with 10% ethyl acetate–hexane gave the *dimethoxy*-β-*tetralone* (3c). It crystallized from ethyl acetate–hexane (0.40 g), m.p. 87—89 °C (Found: C, 72.85; H, 7.05. $C_{15}H_{18}O_3$ requires C, 73.15; H, 7.37%); $\nu_{max.}$ 1 700 (CO) and 1 600 (aromatic) cm^{-1}; $\delta(CDCl_3)$ 2.04—3.04 (8 H, ring CH_2), 3.44 (3 H; 3-OMe), 3.5 (2 H, s, 6-CH_2), 3.84 (3 H, s, 5-OMe), 4.84 (1 H, t, *J* 6 Hz, 3-H), and 6.82 (1 H, s, aromatic).

Procedure B. The crude product (9.0 g) from the Birch reduction of the tricyclic phenol (1), potassium carbonate (20 g), acetone (250 ml), and methyl iodide (9.0 ml) were mixed and stirred for 26 h. Acetone was distilled off, and the mixture was diluted with water and extracted with ether. The extract was treated with oxalic acid (1.5 g) in methanol (150 ml) and the mixture warmed on a steam-bath for 1 h. After evaporating off most of the solvent, the residue was extracted with ether. Chromatography of the extract (8.95 g) on silica gel yielded three fractions. Elution with 5% ethyl acetate–hexane gave fractions 1 and 2. The remaining material was removed by elution with ethyl acetate (fraction 3). The major product, β-tetralone (3c) (3.4 g), appeared in the second fraction. It was crystallized from ethyl acetate–hexane, m.p. 87—89 °C. The first and third fractions afforded the companion products described below.

5-*Methoxy*-2,3,8,9-*tetrahydro*-1H-*cyclopenta*[a]*naphthalen*-7(6H)-*one* (5).—Fraction 1 (0.24 g) referred to in the preceding experiment gave after crystallization from ethyl acetate–hexane the deoxygenated product β-tetralone (5), m.p. 84—85 °C (lit.,[4] 83—84 °C); $\nu_{max.}$ (Nujol) 1 715 (CO), 1 605, and 1 595 (aromatic) cm^{-1}. It gave a yellow 2,4-dinitrophenylhydrazone, m.p. 233—235 °C (lit.,[4] 235—236 °C).

3-*Acetoxy*-7-*methoxy*-2,3,3a,9b-*tetrahydro*-1H-*cyclopenta*[a]*naphthalen*-5(4H)-*one* (4).—Fraction 3 (3.6 g) mentioned above was subjected to t.l.c. analysis, which showed it to be a complex mixture. It was treated with pyridine (30 ml) and acetic anhydride (3 ml) and the mixture was left at 0—5 °C overnight. The acetylated material (2.9 g), obtained after the usual work-up, was chromatographed on silica gel (25 g). Elution with 10% ethyl acetate–hexane yielded the α-tetralone (4) (0.67 g), identical with that described earlier.

3,5-*Dimethoxy*-6-*methyl*-2,3,8,9-*tetrahydro*-1H-*cyclopenta*[a]*naphthalen*-7(6H)-*one* (6).—To sodium methoxide [from sodium (0.184 g) dissolved in methanol (3 ml)], the β-tetralone (3c) (1.968 g) in dry benzene (40 ml) was added under a nitrogen atmosphere with stirring and cooling to 0—5 °C. The contents were stirred for 15—20 min. On adding methyl iodide (1.141 g) in benzene (5 ml) the reaction mixture became bright red, the colour fading during the reaction period (3.5 h). Aqueous oxalic acid was added and the mixture extracted with ether. The crude extract (2.15 g) was chromatographed on a silica gel column (60 g) and eluted with benzene. The first fraction yielded 3,5-*dimethoxy*-6-*methyl*-2,3,8,9-*tetrahydro*-1H-*cyclopenta*[a]*naphthalen*-7(6H)-*one* (6) (1.3 g). It crystallized from benzene–hexane as colourless plates, m.p. 63—64 °C (Found: C, 74.25; H, 8.15. $C_{16}H_{20}O_3$ requires C, 73.82; H, 7.74%); $\nu_{max.}$ (Nujol) 1 725 (CO), 1 610, 1 575, and 1 515 (aromatic) cm^{-1}; $\delta(CDCl_3)$ 1.20 (3 H, d, *J* 6 Hz, Me), 2.0—3.06 (8 H, ring CH_2), 3.36 (3 H, s, 3-OMe), 3.76 (4 H, s, 5-OMe + 6-H), 4.72 (1 H, d, *J* 3 Hz, 3-H), and 6.78 (1 H, s, aromatic).

11,17ξ-*Dimethoxy*-18-*norandrosta*-4,8,11,13-*tetraen*-3-*one* (7a).—To sodium methoxide solution [from sodium (0.23 g) dissolved in methanol (5 ml)] the methylated β-tetralone (6) (1.3 g) dissolved in dry benzene (30 ml) was added. The contents were stirred and cooled under a nitrogen atmos-

phere for 20 min. Methyl vinyl ketone (0.425 g) in benzene (5 ml) was then added and the reaction mixture was stirred for a further 3 h with continued cooling. After acidification with dilute oxalic acid, the mixture was extracted with ether. Chromatography of the extract on a silica gel column (60 g) yielded two fractions; the first fraction eluted with 10% ethyl acetate–hexane and the second with 15% ethyl acetate–hexane. The first fraction (0.6 g) gave, on crystallization from ethyl acetate–hexane, 11,17ξ-*dimethoxy*-18-*norandrosta*-4,8,11,13-*tetraen*-3-*one* (7a) as colourless plates, m.p. 123—124 °C (Found: C, 76.7; H, 7.7. $C_{20}H_{24}O_3$ requires C, 76.89; H, 7.74%); $\nu_{max.}$ (Nujol) 1 675 (conjugated CO), 1 625 (alkene), 1 605 and 1 595 (aromatic) cm^{-1}; $\lambda_{max.}$ (EtOH) 210 (ε 23 710), 232 (ε 22 310), and 288 (ε 3 835) nm; δ($CDCl_3$) 1.68 (3 H, s, 19-Me), 1.76—3.16 (12 H, CH_2), 3.42 (3 H, s, 17-OMe), 3.88 (3 H, s, aromatic OMe), 4.76 (1 H, t, *J* 2 Hz, 17-H), 5.78 (1 H, s, vinyl), and 6.82 (1 H, s, aromatic).

3,5-*Dimethoxy*-6-*methyl*-2,3,8,9-*tetrahydro*-6,8-(10-*hydroxy*-(10-*methylpropano*)-1H-*cyclopenta*[a]*naphthalen*-7(6H)-*one* (8a).—The second fraction (0.61 g) mentioned above, eluted with 15% ethyl acetate-hexane, on crystallization from ethyl acetate-hexane afforded the pure *ketol* (8a), as colourless plates; m.p. 148—150 °C (Found C, 72.35; H, 7.55. $C_{20}H_{26}O_4$ requires C, 72.16; H, 7.93%). $\nu_{max.}$ (Nujol) 3 400 (OH), 1 705 (CO), 1 600 (aromatic) cm^{-1}. δ($CDCl_3$) 1.28 (3 H, s, 6-Me); 1.48 (3 H, s; 1-Me), 1.74 (1 H, s, D-exchangeable; -OH), 1.42—3.02 (11 H; methylene, methine protons) 3.42 (3 H, d; 1-OMe), 3.82 (3 H, s; 6′-OMe), 4.76 (1 H, t, *J* 4 Hz; 1′-H), 6.84 (1 H, s, aromatic).

Androstatetraenone (7a) *from Ketol* (8a).—Ketol (8a) (0.5 g) was added to 10% methanolic potassium hydroxide (40 ml) and the mixture was refluxed for 15 min. Acidification gave virtually a single product which was further purified by chromatography on a silica gel column and crystallization from ethyl acetate-hexane (0.240 g), m.p. 123—124 °C. It was identical with the enone (7a) obtained earlier in all respects. In contrast, when a solution of the ketol (8a) in methanolic hydrochloric acid was refluxed for 6 h and the solution concentrated, the compound was recovered unchanged.

11,17ξ-*Dimethoxygona*-4,8,11,13-*tetraen*-3-*one* (7b).—3,5-Dimethoxy-2,3,8,9-tetrahydro-1*H*-cyclopenta[*a*]naphthalen-7(6*H*)-one (3c) (1.0 g) was dissolved in benzene (25 ml) and the solution added to sodium methoxide solution (0.20 g sodium dissolved in 3 ml methanol) with stirring and cooling at 0—5 °C under a nitrogen atmosphere. After 20 min a solution of methyl vinyl ketone (0.32 g) in benzene (10 ml) was added. Stirring was continued for 3 h more. The solution was acidified, extracted with ether and dried over sodium sulphate. The crude extract (1.43 g) was chromatographed on a silica gel column. Elution with 10% ethyl acetate-hexane yielded 11,17ξ-*dimethoxygona*-4,8,11,13-*tetraen*-3-*one* (7b) (0.32 g); needles from ethyl acetate-hexane, m.p. 140—143 °C (Found C, 76.15; H, 7.6. $C_{19}H_{22}O_3$ requires C, 76.48; H, 7.43%); $\nu_{max.}$ (Nujol) 1 675 (conjugated carbonyl), 1 625 (alkene) and 1 590 (aromatic) cm^{-1}; $\lambda_{max.}$ (EtOH) 215 (ε 13 000), 233 (ε 21 500), 291 (ε 1 800) nm, δ($CDCl_3$) 1.52—3.06 (12 H, CH_2), 3.44 (3 H, s, 17-OMe), 3.90 (4 H, s, merged signal for 11-OMe and 17-H), 4.82 (1 H, t, *J* 4 Hz; 17-H), 5.98 (1 H, q, *J* 2 Hz, vinyl), and 6.82 (1 H, s, aromatic).

3,5-*Dimethoxy*-2,3,8,9-*tetrahydro*-6,8-(10-*hydroxy*-10-*methylpropano*)-1H-*cyclopenta*[a]*naphthalen*-7(6H)-*one* (8b).—The column described in the last experiment was eluted further with ethyl acetate-hexane (1 : 4) to give the *ketol* (8b) (0.70 g) which crystallized from benzene, m.p. 150—152 °C (Found C, 72.95; H, 6.62. $C_{19}H_{24}O_4$ requires C, 73.06; H, 6.45%); $\nu_{max.}$ (Nujol) 3 400 (OH), 1 710 (CO), and 1 600 (aromatic) cm^{-1}; δ($CDCl_3$) 1.40 (3 H, s, 6-Me), 1.96 (1 H, s, D-exchangeable; 6-OH), 1.16—3.04 (11 H, ring CH_2 and CH), 3.48 (3 H, s, 1′-OMe), 3.82 (4 H, s, merged signal for 6′-OMe and 1′-H), 4.80 (1 H, t, *J* 6 Hz, 1′-H), and 6.82 (1 H, s, aromatic).

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