5. *Modified Steroid Hormones. Part XXVI.* Some 6-Methylated Aromatic Types.*

By D. Burn, V. Petrow, and G. Weston.

Extension of the dienone–phenol rearrangement to certain 6-methylated 1,4-dien- and 1,4,6-trien-3-ones is reported.

Our studies on 6-methylated steroid hormones are herein extended to some aromatic types.†

Initially we examined an approach involving 6-methylation of a suitable aromatic intermediate. To this end cholest-4-ene-3,6-dione was dehydrogenated with 2,3-dichloro-5,6-dicyanobenzoquinone [2] with formation of cholesta-1,4-diene-3,6-dione (I), rearrangement of which with acetic anhydride and toluene *p*-sulphonic acid, followed by alkaline hydrolysis of the resulting enol acetate, afforded 3-hydroxy-1-methyl-19-norcholesta-1,3,5(10)-trien-6-one (II; R = H). The overall yield of the 6-oxo-derivative (II) was however, so low that its conversion into a 6-methylated derivative by reaction with methylmagnesium iodide was not thought worthy of examination.

We next turned to the dienone–phenol rearrangement of a 6-methylated intermediate. Bromination of 5α,6β-dihydroxy-6α-methylcholestan-3-one [3] (III; R = H) gave the 2α-bromo-derivative (III; R = Br), which on acid-catalysed dehydration, followed by elimination of hydrogen bromide by lithium chloride in dimethylformamide, afforded

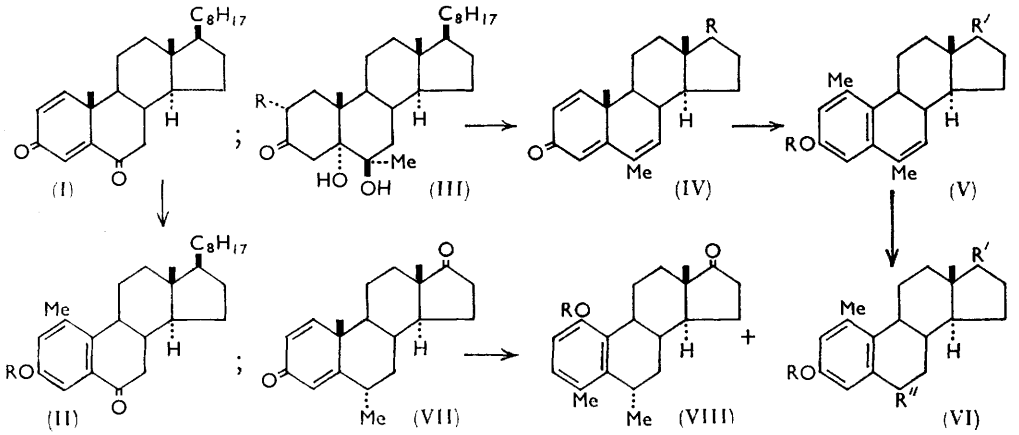
* Part XXV, preceding paper.

† A recent publication [1] from the Syntex Laboratories describes the preparation, by an alternative route, of 6-methylated œstrogens, lacking the 1-methyl substituent.

[1] Velarde, Iriarte, Ringold, and Djerassi, *J. Org. Chem.*, 1959, **24**, 311.
[2] Burn, Kirk, and Petrow, *Proc. Chem. Soc.*, 1960, 14.
[3] Ellis, Kirk, Petrow, Waterhouse, and Williamson, *J.*, 1960, 2828.

6-methylcholesta-1,4,6-trien-3-one (IV; R = C_8H_{17}). The last compound was subsequently and more conveniently obtained by dehydrogenation of 6-methylcholesta-4,6-dien-3-one with the dichlorodicyanoquinone. Its dienone–phenol rearrangement with acetic anhydride and toluene *p*-sulphonic acid furnished 3-acetoxy-1,6-dimethyl-19-norcholesta-1,3,5(10),6-tetraene (V; R = Ac, R′ = C_8H_{17}) in satisfactory overall yield.

Extension of this process to 6-methylandrosta-4,6-diene-3,17-dione [3] furnished the



1,4,6-triene (IV; R = O), which was rearranged to give, after hydrolysis, 3-hydroxy-1,6-dimethyl-œstra-1,3,5(10),6-tetraene-17-one (V; R = H, R′ = O), characterised as its acetate and 3-methyl ether. 17β-Acetoxy-6-methylandrosta-1,4,6-trien-3-one (IV; R = —OAc, • • • H) similarly gave the 3,17β-diacetate (V; R = Ac, R′ = —OAc, • • • H), also obtained from the 17-one (V; R = H, R′ = O), by reduction with sodium borohydride followed by acetylation.

Catalytic hydrogenation of the foregoing 6,7-dehydrophenols (V; R = Ac, R′ = —OAc, • • • H or R′ = O) led to products assigned the 6β-methyl configuration (VI; R = Ac, R′ = —OAc, • • • H or O, R″ = —Me, • • • H) in conformity with the generally observed addition of hydrogen to the α-face of the molecule under conditions of catalytic hydrogenation. In addition, the 17-ketone (VI; R = Ac, R′ = O, R″ = —Me, • • • H) differed from the authentic 6α-methyl epimer (VI; R = Ac, R′ = O, R″ = • • • Me, —H) which was obtained in the following way. 6α-Methylandrost-4-ene-3,17-dione [4] was converted into its 1-dehydro-derivative (VII) with the dichlorodicyanoquinone. Reaction with hydrobromic acid [5] led to a mixture of the required 6α-methylphenol (VI; R = H, R′ = O, R″ = • • • Me, —H) and the 6α-methyl-1-phenol (VIII; R = H), which were readily separated, after saponification, by virtue of their contrasting solubilities in alkali. The acetate of the 1-phenol was the sole product when acetic anhydride and toluene-*p*-sulphonic acid were used to effect the rearrangement.[6]

6-Methylpregna-4,6-diene-3,20-dione [7] was similarly converted into the 1,4,6-trien-3-one (IV; R = —COMe, • • • H), which was rearranged and then hydrolysed to 3-hydroxy-1,6-dimethyl-19-norpregna-1,3,5(10),6-tetraen-20-one (V; R = H, R′ = —COMe, • • • H). Catalytic hydrogenation afforded the corresponding dihydro-6β-methyl derivative (VI; R = H, R′ = —COMe, • • • H, R″ = —Me, • • • H).

Experimental

M. p.s are corrected. Optical rotations were determined for " AnalaR " chloroform solutions, unless otherwise stated. Ultraviolet spectra (in EtOH) were kindly determined by

[4] Ackroyd, Adams, Ellis, Petrow, and Stuart-Webb, *J.*, 1957, 4099.
[5] Dreiding, Pummer, and Tomasewski, *J. Amer. Chem. Soc.*, 1953, **75**, 3159.
[6] Woodward and Singh, *J. Amer. Chem. Soc.*, 1950, **72**, 494.
[7] Ruggieri, Ferrani, and Gandolfi, *Ann. Chim.* (*Italy*), 1959, **49**, 1371.

Mr. M. T. Davies, B.Sc., and Miss D. F. Dobson, B.Sc. B.D.H. Alumina (chromatographic grade) was used throughout.

Cholesta-1,4-diene-3,6-dione (I).—A solution of cholest-4-ene-3,6-dione (3 g.) and 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (2 g.) in dry dioxan (20 ml.) was heated under reflux for 7 hr. The precipitated quinol was removed and the product was isolated with ether. Crystallisation from hexane gave *cholesta-1,4-diene-3,6-dione* as laths, m. p. 132—134°, $[\alpha]_D^{22}$ −90·5° (*c* 1·05), $\lambda_{max.}$ 251 mμ (ε 14,800) (Found: C, 81·65; H, 10·2. $C_{27}H_{40}O_2$ requires C, 81·7; H, 10·2%).

3-Hydroxy-1-methyl-19-norcholesta-1,3,5(10)-trien-6-one (II; R = H).—A solution of cholesta-1,4-diene-3,6-dione (1·6 g.) and toluene-*p*-sulphonic acid (0·5 g.) in acetic anhydride (50 ml.) was kept at 100° for 7 hr. The mixture was poured into ice-water, and the product was isolated with dichloromethane. Hydrolysis with concentrated hydrochloric acid (0·5 ml.) in ethanol (25 ml.) at room temperature for 4 hr. and isolation with ether afforded a gum which was chromatographed on alumina (25 g.) in benzene. Elution with methanol–ether (1 : 9) and crystallisation from methanol gave *3-hydroxy-1-methyl-19-norcholesta-1,3,5(10)-trien-6-one* as rods, m. p. 200—202°, $[\alpha]_D^{20}$ +68·5° (*c* 0·4), $\lambda_{max.}$ 225 (ε 18,600), 261·5 (ε 7630), and 326 mμ (ε 2890) (Found: C, 81·25; H, 9·85. $C_{27}H_{40}O_2$ requires C, 81·7; H, 10·2%). The *acetate* (II; R = Ac) (obtained by using acetic anhydride and pyridine) separated from aqueous acetone in prisms, m. p. 119—120°, $[\alpha]_D^{27}$ +60·5° (*c* 1·05), $\lambda_{max.}$ 251 (ε 9080) and 302 mμ (ε 1985) (Found: C, 79·1; H, 9·4. $C_{29}H_{42}O_3$ requires C, 79·4; H, 9·65%).

2α-Bromo-5α,6β-dihydroxy-6α-methyl-5α-cholestan-3-one (III; R = Br).—Bromine (1·4 g.) in dioxan (14 ml.) was added with stirring to 5α,6β-dihydroxy-6α-methyl-5α-cholestan-3-one (3·5 g.) in dioxan (100 ml.). The solid obtained on pouring the mixture into water was collected and crystallised from acetone–hexane to give the *bromo-ketone* as needles, m. p. 200—201°, $[\alpha]_D^{20}$ +20° (*c* 0·75) (Found: C, 66·1; H, 9·35; Br, 15·0. $C_{28}H_{47}O_3Br$ requires C, 65·75; H, 9·25; Br, 15·6%).

2α-Bromo-6-methylcholesta-4,6-dien-3-one.—The foregoing bromo-ketone (4 g.) was heated with ethanol (200 ml.) containing concentrated hydrochloric acid (1·25 ml.) under reflux for 2 hr. and the solution evaporated to small bulk. The product was isolated with ether and crystallised from dichloromethane–methanol to give the *bromo-dienone* as prisms, m. p. 165° (decomp.), $[\alpha]_D^{21}$ +106° (*c* 1·1), $\lambda_{max.}$ 294 mμ (ε 22,400) (Found: C, 71·05; H, 9·15; Br, 16·3. $C_{28}H_{43}OBr$ requires C, 70·75; H, 9·1; Br, 16·8%).

6-Methylcholesta-1,4,6-trien-3-one (IV; R = $-C_8H_{17}$, ···H).—(*a*) A solution of the foregoing bromo-dienone (4·7 g.) and lithium chloride (3 g.) in dimethylformamide (50 ml.) was heated under reflux and under nitrogen for 1·5 hr. After evaporation of most of the solvent under reduced pressure, the product was isolated with ether and chromatographed on alumina (50 g.) in light petroleum (b. p. 40—60°). Benzene–light petroleum (1 : 3 and 1 : 2) eluted gums which crystallised from hexane, on cooling in acetone–solid carbon dioxide, to give the *trienone* as flakes, m. p. 67—68°, $[\alpha]_D^{22}$ −12·5° (*c* 0·8), $\lambda_{max.}$ 228 (ε 9910), 257 (ε 8850), and 303 mμ (ε 10,500) (Found: C, 84·95; H, 10·75. $C_{28}H_{42}O$ requires C, 85·2; H, 10·75%).

(*b*) A solution of 6-methylcholesta-4,6-dien-3-one (5 g.) and the quinone (4 g.) in dry dioxan (50 ml.) was refluxed for 4 hr. The product was isolated with ether and crystallised from hexane, to give the trienone, m. p. 66—67°, identical with that prepared by method (*a*).

3-Acetoxy-1,6-dimethyl-19-norcholesta-1,3,5(10),6-tetraene (V; R = Ac, R′ = $-C_8H_{17}$, ···H).—A solution of the foregoing trienone (1 g.) and toluene-*p*-sulphonic acid (0·3 g.) in acetic anhydride (30 ml.) was kept at 100° for 4 hr. The product was isolated with ether and crystallised from chloroform–ethanol to give the *acetate* as needles, m. p. 146—147°, $[\alpha]_D^{22}$ −73·1° (0·65), $\lambda_{max.}$ 224·5 (ε 28,210), 231 (ε 25,329), and 266 mμ (ε 8696) (Found: C, 83·2; H, 10·45. $C_{30}H_{44}O_2$ requires C, 83·25; H, 10·25%).

6-Methylandrosta-1,4,6-triene-3,17-dione (IV; R = O).—A solution of 6-methylandrosta-4,6-diene-3,17-dione (7·5 g.) and the quinone (6·2 g.) in dry benzene (150 ml.) was refluxed for 6 hr. The product was isolated with ether and crystallised from acetone–hexane to give the *triene-dione* as prisms, m. p. 219—221°, $[\alpha]_D^{22}$ +84° (*c* 0·2), $\lambda_{max.}$ 227 (ε 12,720), 250 (ε 9050), and 301 mμ (ε 11,720) (Found: C, 80·9; H, 8·4. $C_{20}H_{24}O_2$ requires C, 81·1; H, 8·2%).

3-hydroxy-1,6-Dimethyl-œstra-1,3,5(10),6-tetraen-17-one (V; R = H, R′ = O).—A solution of the foregoing triene-dione (11 g.) and toluene-*p*-sulphonic acid (3 g.) in acetic anhydride (300 ml.) was kept at 100° for 7 hr. The product was isolated with ether and heated for 1 hr. with sodium hydroxide (10 g.) in methanol (300 ml.) and water (50 ml.). The solution was

diluted with water, then acidified with dilute sulphuric acid, and the product isolated with chloroform. Crystallisation from acetone–hexane gave the *phenol* as needles, m. p. 190—192°, $[\alpha]_D^{20}$ −47·5° (*c* 1·0), $\lambda_{max.}$ 225 (ε 28,200), 265 (ε 7590), 273 (ε 6310) and 305 mμ (ε 2190) (Found: C, 80·8; H, 8·1. $C_{20}H_{24}O_2$ requires C, 81·1; H, 8·2%).

The *acetate* (V; R = Ac, R′ = O) (prepared by acetic anhydride–pyridine overnight at room temperature) formed needles (from aqueous methanol), m. p. 105—107°, $[\alpha]_D^{21}$ −39° (*c* 0·6), $\lambda_{max.}$ 223·5 (ε 28,500), 229·5 (ε 25,100), and 266 mμ (ε 8130) (Found: C, 77·95; H, 7·4. $C_{22}H_{26}O_3$ requires C, 78·05; H, 7·7%).

The *methyl ether* (V; R = Me, R′ = O) (formed by dimethyl sulphate–sodium hydroxide) formed needles (from methanol), m. p. 129—130°, $[\alpha]_D^{20}$ −38·5° (*c* 0·8), $\lambda_{max.}$ 225·5 (ε 33,990), 264·5 (ε 8164), and 302 mμ (ε 2263) (Found: C, 81·45; H, 8·35. $C_{21}H_{26}O_2$ requires C, 81·25; H, 8·4%).

17β-*Acetoxy*-6-*methylandrosta*-1,4,6-*trien*-3-*one* (IV; R = —OAc, • • • H).—A solution of 17β-acetoxy-6-methylandrosta-4,6-dien-3-one [4] (3 g.) and the quinone (3 g.) in dry dioxan (30 ml.) was refluxed for 3 hr. and the product isolated with ether. Crystallisation from hexane gave the *trienone* as prisms, m. p. 148—149°, $[\alpha]_D^{25}$ −18° (*c* 0·85), $\lambda_{max.}$ 228·5 (ε 17,900), 250—255 (ε 9020), and 302 mμ (ε 12,100) (Found: C, 77·4; H, 8·3. $C_{22}H_{28}O_3$ requires C, 77·6; H, 8·3%).

3,17β-*Diacetoxy*-1,6-*dimethylœstra*-1,3,5(10),6-*tetraene* (V; R = Ac, R′ = —OAc, • • • H).—(*a*) A solution of the foregoing trienone (2·75 g.) and toluene-*p*-sulphonic acid (0·8 g.) in acetic anhydride (25 ml.) was kept at 100° for 9 hr. The product, isolated with ether, was filtered through alumina (50 g.) in light petroleum (b. p. 40—60°) and crystallised from aqueous methanol, to give the *diacetate* as rods, m. p. 115—116°, $[\alpha]_D^{20}$ −112·5° (*c* 0·55), $\lambda_{max.}$ 223·5 (ε 28,200), 229·5 (ε 25,700), and 265 mμ (ε 8510) (Found: C, 75·2; H, 8·15. $C_{24}H_{30}O_4$ requires C, 75·35; H, 7·9%).

(*b*) A solution of the 17-ketone (V; R = H, R′ = O) (1·5 g.) and sodium borohydride (0·2 g.) in methanol (20 ml.) was kept overnight at room temperature. After acidification with dilute hydrochloric acid, the steroid was precipitated with water and isolated with chloroform. Crystallisation from acetone–hexane and dichloromethane–methanol gave 3,17β-*dihydroxy*-1,6-*dimethylœstra*-1,3,5(10),6-*tetraene* (IV; R = H, R′ = —OH, • • • H) as prisms, m. p. 128—129°, $[\alpha]_D^{21}$ −89·5° (*c* 0·65), $\lambda_{max.}$ 225 (ε 27,500), 265 (ε 7760), and 303—307 mμ (ε 2350) (Found: C, 76·05; H, 9·2. $C_{20}H_{26}O_2,H_2O$ requires C, 75·9; H, 8·9%). Acetylation with acetic anhydride–pyridine overnight at room temperature and crystallisation from aqueous methanol afforded the diacetate, m. p. 114—116°, identical with that prepared as under (*a*) above.

17β-*Acetoxy*-3-*methoxy*-1,6-*dimethyl*-*œstra*-1,3,5(10),6-*tetraene* (V; R = Me, R′ = —OAc, • • • H).—Treatment of the foregoing diol (1 g.) with alkaline dimethyl sulphate gave the 3-methyl ether which resisted crystallisation. With acetic anhydride–pyridine at room temperature overnight this gave the *methyl ether* 17-*acetate*, needles (from dichloromethane–methanol), m. p. 162—163°, $[\alpha]_D^{20.5}$ −126·5° (*c* 0·8), $\lambda_{max.}$ 225·5 (ε 29,530), 265·5 (ε 7550), and 302 mμ (ε 2160) (Found: C, 77·7; H, 8·4. $C_{23}H_{30}O_3$ requires C, 77·9; H, 8·5%).

3-*Acetoxy*-1,6β-*dimethylœstra*-1,3,5(10)-*trien*-17-*one* (VI; R = Ac, R′ = O, R″ = —Me, • • • H).—The Δ⁶-acetoxy-ketone (V; R = Ac, R′ = O) (0·5 g.) was hydrogenated at N.T.P. in methanol (50 ml.) over 2% palladium–barium carbonate (0·15 g.) until 1 mol. of hydrogen had been adsorbed. The catalyst was removed and the solution diluted with water. Crystallisation of the product from aqueous methanol gave the *acetoxy*-6β-*methyl ketone* as prisms, m. p. 155—156°, $[\alpha]_D^{26}$ +178·5° (*c* 1·0), $\lambda_{max.}$ 269 mμ (ε 363) (Found: C, 77·55; H, 8·25. $C_{22}H_{28}O_3$ requires C, 77·6; H, 8·30%).

This acetate (0·5 g.) with boiling aqueous-methanolic sodium hydroxide gave after 1 hr. the *hydroxy*-6β-*methyl ketone* (VI; R = H, R′ = O, R″ = —Me, • • • H), flakes (from aqueous methanol), m. p. 202—204°, $[\alpha]_D^{20}$ +208·5° (*c* 0·5), $\lambda_{max.}$ 286 mμ (ε 200) (Found: C, 80·7; H, 8·8. $C_{20}H_{26}O_2$ requires C, 80·5; H, 8·8%).

Methylation with dimethyl sulphate and alkali then gave the *methoxy*-6β-*methyl ketone* (VI; R = Me, R′ = O, R″ = —Me, • • • H), prisms (from aqueous methanol, m. p. 150—152°, $[\alpha]_D^{21}$ +213·5° (*c* 1·2), $\lambda_{max.}$ 279 (ε 1736) and 286 mμ (ε 1771) (Found: C, 80·2; H, 8·9. $C_{21}H_{28}O_2$ requires C, 80·7; H, 9·0%).

3,17β-*Diacetoxy*-1,6β-*dimethylœstra*-1,3,5(10)-*triene* (VI; R = Ac, R′ = —OAc, • • • H, R″ = —Me, • • • H).—The 6-dehydro-diacetate (V; R = Ac, R′ = —OAc, • • • H) (0·5 g.) was hydrogenated at N.T.P. in methanol (50 ml.) over 2% palladium–calcium carbonate (0·2 g.). The product was isolated with ether and crystallised from aqueous methanol to give the *diacetate*

(VI) as rods, m. p. 95—96°, $[\alpha]_D^{21}$ +69° (*c* 0·55), $\lambda_{max.}$ 269 mμ (ε 408) (Found: C, 74·9; H, 8·35. $C_{24}H_{32}O_4$ requires C, 74·95; H, 8·4%). The corresponding diol did not crystallise.

6α-*Methylandrosta*-1,4-*diene*-3,17-*dione* (VII).—A solution of 6α-methylandrost-4-ene-3,17-dione (5 g.) and the quinone (4 g.) in dry benzene (50 ml.) was heated under reflux for 12 hr. After removal of the quinol, the product was isolated with ether and crystallised from acetone–hexane to give the *diene-dione* as prisms, m. p. 219—221°, $[\alpha]_D^{20}$ +103° (*c* 0·3), $\lambda_{max.}$ 243 mμ (ε 14,540) (Found: C, 80·3; H, 8·65. $C_{20}H_{26}O_2$ requires C, 80·5; H, 8·8%).

3-*Hydroxy*-1,6α-*dimethyl*- (VI; R = H, R′ = O, R″ =···Me, —H) *and* 1-*Hydroxy*-4,6α-*dimethyl*-*œstra*-1,3,5(10)-*trien*-17-*one* (VIII; R = H).—The foregoing diene-dione (3·6 g.) and 50% aqueous hydrobromic acid (50 ml.) were kept at 75° for 7½ hr. The solid which had separated was collected and digested with hot 5% aqueous sodium hydroxide for 2 hr. The alkali-soluble portion was precipitated with dilute acid and crystallised from aqueous methanol to give 3-*hydroxy*-1,6α-*dimethylœstra*-1,3,5(10)-*trien*-17-*one* as plates, m. p. 230—232°, $[\alpha]_D^{22}$ +210° (*c* 0·6), $\lambda_{max.}$ 286 mμ (ε 1820) (Found: C, 80·5; H, 8·85. $C_{20}H_{26}O_2$ requires C, 80·5; H, 8·8%). The *acetate* (VI; R = Ac, R′ = O, R″ =···Me, —H) formed needles (from aqueous methanol), m. p. 128—129°, $[\alpha]_D^{23}$ +205° (*c* 0·4), $\lambda_{max.}$ 270 mμ (ε 354) (Found: C, 77·6; H, 8·05. $C_{22}H_{28}O_3$ requires C, 77·6; H, 8·3%).

The alkali-insoluble portion crystallised from aqueous methanol to give 1-*hydroxy*-4,6α-*dimethylœstra*-1,3,5(10)-*trien*-17-*one* as needles, m. p. 236—238° (depressed on admixture with the 3-hydroxy-1,6α-dimethyl-isomer), $[\alpha]_D^{23}$ +274° (*c* 0·6), $\lambda_{max.}$ 290 mμ (ε 2030) (Found: C, 80·4; H, 8·7. $C_{20}H_{26}O_2$ requires C, 80·5; H, 8·8%).

1-*Acetoxy*-4,6α-*dimethylœstra*-1,3,5(10)-*trien*-17-*one* (VIII; R = Ac).—(*a*) The foregoing 1-phenol (0·5 g.) was acetylated in the usual way and the product was crystallised from aqueous methanol to give the *acetate* as needles, m. p. 167—169°, $[\alpha]_D^{21}$ +246° (*c* 0·85), $\lambda_{max.}$ 279 mμ (ε 360) (Found: 77·7; H, 8·4. $C_{22}H_{28}O_3$ requires C, 77·6; H, 8·3%).

(*b*) A solution of the diene-dione (VII) (3 g.) and toluene-*p*-sulphonic acid (0·8 g.) in acetic anhydride (75 ml.) was kept at 100° for 5 hr. The product was isolated with ether and chromatographed on alumina (50 g.) in light petroleum (b. p. 40—60°), which eluted the acetate (VIII; R = Ac), forming needles (from aqueous methanol), m. p. 166—168°, identical with that obtained as in (*a*) above.

6-*Methylpregna*-1,4,6-*triene*-3,20-*dione* (IV; R = —Ac, ···H).—A solution of 6-methylpregna-4,6-diene-3,20-dione (5 g.) and the quinone (5 g.) in benzene (75 ml.) was refluxed for 4 hr. and the product was isolated with ether. Crystallisation from acetone–hexane gave the *triene-dione* as rods, m. p. 166—168°, $[\alpha]_D^{22}$ +100° (*c* 0·25), $\lambda_{max.}$ 228 (ε 12,240), 303 (ε 10,860), and $\lambda_{infl.}$ 251 mμ (ε 8280) (Found: C, 81·55; H, 8·75. $C_{22}H_{28}O_2$ requires C, 81·4; H, 8·7%).

3-*Hydroxy*-1,6-*dimethyl*-19-*norpregna*-1,3,5(10),6-*tetraen*-20-*one* (V; R = H, R′ = —Ac, ···H).—The foregoing trienedione (3 g.) and toluene-*p*-sulphonic acid (1 g.) in acetic anhydride (80 ml.) were kept at 100° for 7 hr. As the product, isolated with ether, did not crystallise, it was hydrolysed with sodium hydroxide (1 g.) in methanol (25 ml.) and water (10 ml.) overnight at room temperature. The hydrolysed material obtained on pouring the mixture into dilute acetic acid was chromatographed on alumina (50 g.) in benzene. Benzene–ether (4 : 1) eluted gums which crystallised from aqueous methanol to give the *phenol* as flakes, m. p. 205—206°, $[\alpha]_D^{19}$ —34·5° (*c* 0·8), $\lambda_{max.}$ 225 (ε 29,812), 265 (ε 8500), 302 (ε 2695), and $\lambda_{infl.}$ 272·5 mμ (ε 7070) (Found: C, 81·8; H, 8·9. $C_{22}H_{28}O_2$ requires C, 81·4; H, 8·7%).

The *acetate* (V; R = Ac, R′ = —Ac, ···H) formed rods (from methanol), m. p. 160—162°, $[\alpha]_D^{21}$ —34·1° (*c* 0·9), $\lambda_{max.}$ 224 (ε 28,810), 230 (ε 26,350), and 265·5 mμ (ε 8943) (Found: C, 78·4; H, 8·25. $C_{24}H_{30}O_3$ requires C, 78·65; H, 8·25%).

3-*Hydroxy*-1,6β-*dimethyl*-19-*norpregna*-1,3,5(10)-*trien*-20-*one* (VI; R = H, R′ = —Ac, ···H, R″ = —Me, ···H).—The phenol (V; R = H, R′ = —Ac, ···H) (0·4 g.) was hydrogenated at N.T.P. in methanol (50 ml.) over 2% palladium–calcium carbonate (0·15 g.). After removal of the catalyst, the solution was diluted with water, and the product crystallised from aqueous methanol to give the 6β-*methylphenol* as rods, m. p. 185—187°, $[\alpha]_D^{22}$ +203·1° (*c* 0·5), $\lambda_{max.}$ 285·5 (ε 1894) and $\lambda_{infl.}$ 222 mμ (ε 9175) (Found: C, 81·3; H, 8·95. $C_{22}H_{30}O_2$ requires C, 80·9; H, 9·25%).

The *acetate* (VI; R = Ac, R′ = Ac, ···H, R″ = —Me ···H,) formed plates (from aqueous methanol), m. p. 121—122°, $[\alpha]_D^{20}$ +185·6° (*c* 1·0), $\lambda_{max.}$ 269·2 (ε 385) and 273·5 mμ (ε 364) (Found: C, 78·0; H, 8·8. $C_{24}H_{32}O_3$ requires C, 78·2; H, 8·75%).

CHEMICAL RESEARCH LABORATORIES,
THE BRITISH DRUG HOUSES, LTD., LONDON, N.1.

[*Received, July 28th*, 1961.]