Applications of High-potential Quinones. Part VII.[1] The Synthesis of Steroidal Phenanthrenes by Double Methyl Migration

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Steroidal phenanthrenes are formed from 17α-methyl-$\Delta^{9(11)}$-testosterones by the action of dichlorodicyanobenzoquinone and toluene-*p*-sulphonic acid in refluxing dioxan. Initial dehydration occurs without rearrangement to give Δ^{16}-derivatives, which undergo double methyl migration and oxidation to the phenanthrenes. Isolation of the Δ^{16}-intermediates is ascribed to the presence of the $\Delta^{9(11)}$-bond, which eliminates the usual 11β-H–13-Me diaxial interaction in ring C.

DIELS isolated the phenanthrene hydrocarbon (1) from selenium dehydrogenation of cholesterol.[2] Diels' hydrocarbon has since become a standard degradation product for the identification of the steroid nucleus in natural products, and the method has recently been adapted for use on a microscale by g.l.c./m.s.[3] Although a vast number of cyclopenteno- and cyclopentadieno-phenanthrenes have now been obtained from commonly occurring steroids, vigorous reaction conditions are required for the reactions and yields are often low. The standard reagents are selenium and palladium charcoal, used at high temperatures, and simple pyrolysis is also effective in certain circumstances.[4] Dannenberg's use of high-potential quinones, notably chloranil, for the dehydrogenation of steroids allowed the isolation of phenan-

[1] Part VI, W. Brown and A. B. Turner, *J. Chem. Soc.* (*C*), 1971, 2057.

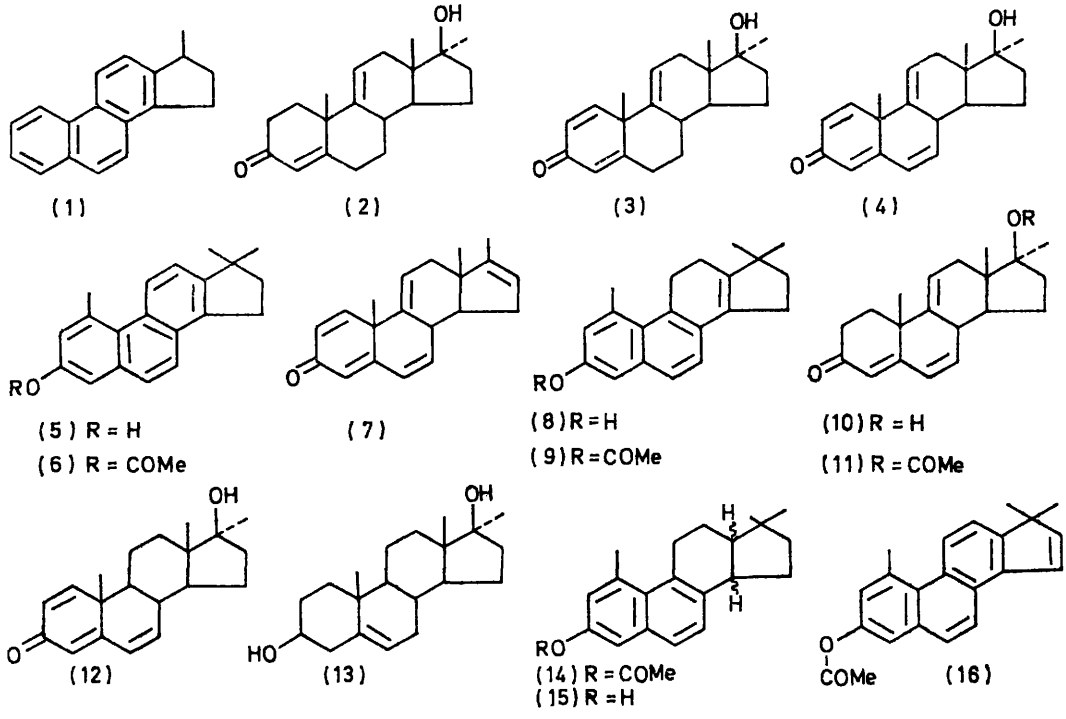
[2] *O. Diels*, W. Gädke and P. Körding, *Annalen*, 1927, **459**, 1.

[3] J. C. Orr, private communication, Hamburg, Sept. 12, 1970.

[4] L. F. Fieser and M. Fieser, ' Steroids,' Reinhold, New York, 1959, pp. 83 *et seq.*

threnes in yields up to 50%.[5] In developing new routes to ring A/B aromatic steroids, we have studied the oxidation of 17α-methyl-$\Delta^{9(11)}$-testosterone (2) by dichlorodicyanobenzoquinone, which gives phenanthrenes under relatively mild conditions.[6]

Initial dehydrogenation of the testosterone (2) with the quinone in boiling dioxan gave the expected 1,2-dehydro-derivative (3) in 84% yield. This compound has previously been prepared by the bromination–dehydrobromination sequence,[7] and by microbiological dehydrogenation using *Bacillus sphaericus*.[8] Physical data on the material obtained by the quinone method suggested that it was contaminated with a small amount of the tetraenone (4), which could not be removed. Further dehydrogenation of the trienone (3) by dichlorodicyanobenzoquinone took place readily in the presence of toluene-*p*-sulphonic acid. This catalyst is required to promote enolisation of $\Delta^{1,4}$-3-ketones in quinone dehydrogenation to $\Delta^{1,4,6}$-3-ketones.[9] After 72 hr. in boiling dioxan, two equivalents of the quinone had been consumed, and the only steroidal product was the optically inactive phenanthrene (5) resulting from migration of both angular methyl groups. The structure of the rearranged product (5), which was isolated in 48% yield, was clear from its n.m.r. spectrum. This revealed the presence of a highly deshielded aromatic methyl group (τ 6·98) and a *gem*-dimethyl group (τ 8·65), and the only other aliphatic protons were the two multiplets centred at τ 6·73 and 7·95, which correspond to the methylene groups in ring D.[10] The aromatic proton at C-11 * resonates at much lower field than the other aromatic protons because it alone experiences the deshielding effects of the π-electrons of all three rings. Other physical data was consistent with literature values [11] for the phenol (5), and it readily gave the monoacetate (6) upon acetylation.



When the hydrogen transfer reaction was interrupted after 24 hr., the pentaene (7) was obtained as an oil in 58% yield after chromatography on silica gel. The structure of this intermediate was clear from its spectral properties. In particular, its n.m.r. spectrum exhibited a multiplet for the C-16-olefinic proton at τ 4·65, allylically coupled with the C-17-methyl protons (τ 8·34). The possible presence of an additional tetrasubstituted double bond at the 8(14)-position was ruled out on the basis of its u.v. spectrum, which showed no absorption maximum above 303 nm. An absorption maximum would be expected at *ca.* 348 nm, if the compound

* Steroid numbering retained throughout for the phenanthrenes.

[5] H. Dannenberg, H. Scheurlen, and D. Dannenberg-von Dresler, *Z. physiol. Chem.*, 1956, **303**, 282; H. Dannenberg and H. G. Neumann, *Chem. Ber.*, 1961, **94**, 3085, 3094; *Annalen*, 1964, **675**, 109; H. Dannenberg and K. F. Hebenbrock, *ibid.*, 1966, **700**, 106.

[6] Preliminary communication, W. Brown and A. B. Turner, *Chem. Comm.*, 1968, 561.

[7] U.S.P. 2,793,218 and 2,837,517; G.P. 1,137,010.

[8] U.S.P. 2,899,447; C. H. Robinson, L. E. Finckenor, R. Tiberi, M. Eisler, R. Neri, A. Watnick, P. L. Perlman, P. Holroyd, W. Charney, and E. P. Oliveto, *J. Amer. Chem. Soc.*, 1960, **82**, 4611.

[9] A. B. Turner and H. J. Ringold, *J. Chem. Soc.* (*C*), 1967, 1720.

[10] *Cf.* M. S. Bharucha, E. Weiss, and T. Reichstein, *Helv. Chim. Acta*, 1962, **45**, 103; A. D. Cross and L. J. Durham, *J. Org. Chem.*, 1965, **30**, 3200.

[11] S. Kaufman, *J. Org. Chem.*, 1963, **28**, 1390.

possessed the $\Delta^{1,4,6,8(14)}$-3-one chromophore. The pentaenone (7) could not be crystallised, and was readily transformed into the crystalline phenol (5) after treatment with charcoal in ethyl acetate. An aerial oxidation step is apparently involved in this process.

When the trienone (3) was heated with toluene-*p*-sulphonic acid in benzene in the absence of quinone, simple dehydration to the Δ^{16}-derivative occurred, as shown by the lack of hydroxy-absorption in the i.r. spectrum of the resulting oil. Although attempts to purify the product again met with no success, its n.m.r. spectrum showed the expected multiplet for the new olefinic proton at τ 4·65, and the olefinic methyl group at τ 8·32. Thus initial dehydration in this case also occurred without rearrangement to give the 1,4,9(11),16-tetraen-3-one.

There are many reports in the literature of reactions involving removal of a 17-hydroxy-group and migration of the angular 13-methyl group to C-17.[12] In all cases in which the 17-hydroxy-group is tertiary, rearrangement occurs and the double bond is generated at the 13,14-position, unless it can appear in conjugation with another unsaturated grouping [13] or aromatic system.[11] The isolation of unrearranged Δ^{16}-derivatives from tertiary 17β-alcohols is unusual, although concerted migration of the angular methyl group cannot occur with these alcohols. It is possible that related rearrangements in the literature could also proceed *via* Δ^{16}-intermediates, but, as the isolation or presence of these compounds has not previously been reported, it seems likely that these reactions involve direct formation of the rearranged Δ^{13}-product from the C-17-carbonium ion. However, both the steroids under discussion here possess a $\Delta^{9(11)}$-bond, which is absent in earlier examples of 13-methyl migration. In a saturated ring C steroid, there is a 1,3-diaxial interaction between the 11β-hydrogen atom and the 13-methyl group which is relieved by Wagner–Meerwein rearrangement. The absence of this modest steric interaction (~0·8 kcal./mole) [14] in $\Delta^{9(11)}$-steroids appears to be sufficient to tip the balance in favour of loss of a 16-proton from the original carbonium ion to give the Δ^{16}-derivative. The influence of sp^2-hybridisation in ring C upon the energetics of the rearrangement process is difficult to assess.

A number of related rearrangements involving migration of the 13-methyl group to C-17, with concomitant formation of a Δ^{13}-bond, have been reported recently.[15] In these, the rearrangement follows elimination of a substituent at C-20, and some, if not all of them, proceed *via* a $\Delta^{17(20)}$-intermediate.

The freshly chromatographed pentaenone (7) undergoes a similar double methyl migration, leading direct to the acetoxyphenanthrene (6), in refluxing acetic anhydride containing toluene-*p*-sulphonic acid. The same crystalline phenanthrene (6) is also the major product of dienone–phenol rearrangement of the tetraenone (4), under identical conditions. However, in this case it is contaminated by the dihydrophenanthrene (9). The latter was obtained as an oil after separation by multiple development on t.l.c. plates. Isolation of a similar mixture of the phenol (5) and its 11,12-dihydro-derivative (8) from reaction of the tetraenone (4) with toluene-*p*-sulphonic acid in refluxing dioxan under nitrogen establishes that this acid catalyses the dehydration and aromatisation of the phenanthrene precursor. This result again indicates that the final step leading to the phenanthrenes is a slow aerial oxidation, although the fact that phenanthrene formation could not be completely prevented under nitrogen suggests that some disproportionation may be taking place.

A scheme for the formation of these phenanthrenes from their various precursors is outlined in Scheme 1, although other possibilities may be considered. The first step involves dehydration to the Δ^{16}-compound, rearrangement of the $\Delta^{1,4,6}$-3-ketone system of which gives a ring A aromatic intermediate. This is followed by migration of the $\Delta^{9(11)}$-bond to the 8,9-position to give the naphthalene system, with aromatisation again providing the driving force. In this process the tertiary hydrogen at C-14 becomes benzylic, thereby facilitating further rearrangement to the dihydrophenanthrene. As this also relieves the considerable strain in the C/D-*trans* ring junction, it is hardly surprising that no trace of the Δ^{16}-A/B-aromatic intermediate is detected. Aerial oxidation at 100°, in a system from which oxygen has not been excluded, then completes the process. In the case of the reaction of the trienone (3) with two equivalents of dichlorodicyanobenzoquinone, the extra equivalent of quinone brings about the final oxidation of the dihydrophenanthrene to the phenanthrene. In keeping with this, Coombs [16] has recently shown that dichlorodicyanobenzoquinone is superior to platinum–charcoal for the dehydrogenation of a series of related dihydrophenanthrenes. This mechanism thus accounts for the observed intermediates and products. It is probable that traces of acetic acid in the ethyl acetate are sufficient to cause the dienone–phenol rearrangement of the pentaenone (7), when it is boiled with activated charcoal, leading to the hydroxyphenanthrene(s) by the same mechanism.

In an alternative approach to the pentaenone (7), 17β-hydroxy-17α-methylandrosta-4,6,9(11)-trien-3-one (10) was prepared from the dienone (2) by two methods: dehydrogenation with chloranil in boiling t-butanol [17]

[12] P. de Mayo, 'Molecular Rearrangements,' Interscience, London, 1964, vol. 2, p. 1021; D. N. Kirk and M. P. Hartshorn, 'Steroid Reaction Mechanisms,' Elsevier, Amsterdam, 1968, pp. 270—271

[13] N. L. Wendler, R. P. Graber, and G. G. Hazen, *Tetrahedron*, 1958, **3**, 144.

[14] *E. L. Eliel*, N. L. Allinger, S. J. Angyal, and G. A. Morrison, 'Conformational Analysis,' Interscience, London, 1965, p. 43.

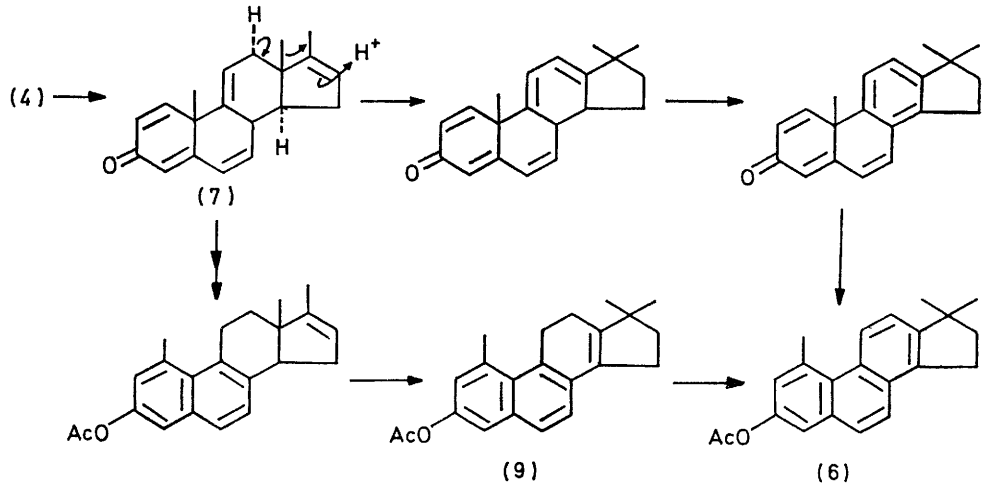
[15] F. Kohen, R. A. Mallory, and I. Scheer, *J. Org. Chem.*, 1971, **36**, 716; H. L. Herzog, O. Gnoj, L. Mandell, G. G. Nathansohn, and A. Vigerani, *J. Org. Chem.*, 1967, **32**, 2906; E. A. Brown, *J. Medicin. Chem.*, 1967, **10**, 546.

[16] M. M. Coombs, S. B. Jaitly, and F. E. H. Crawley, *J. Chem. Soc.* (*C*), 1970, 1266.

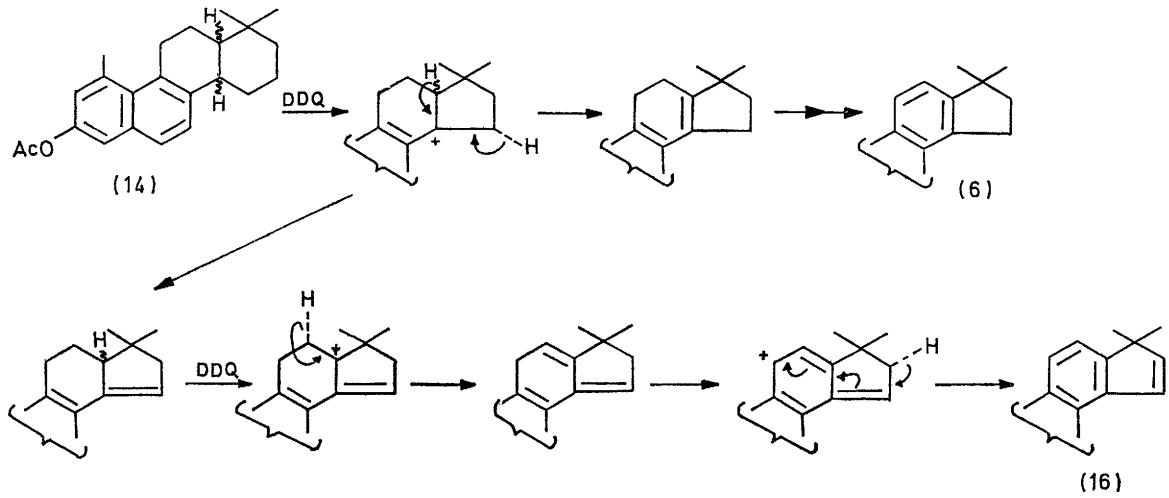
[17] J. A. Campbell and J. C. Babcock, *J. Amer. Chem. Soc.*, 1959, **81**, 4069.

and with dichlorodicyanobenzoquinone catalysed by hydrogen chloride at room temperature.[9] The latter reaction was initially found to be the quicker and cleaner of the two, giving the trienone (10) in 70% yield, whereas only a 50% yield was obtained from the chloranil reaction. Unfortunately, the acid-catalysed reaction was not reproducible, and the product was contaminated with starting material, which was difficult to remove. In pentaenone (7). Its 17β-acetate (11) was prepared in high yield by heating a solution of the alcohol (10) in acetic anhydride under reflux for 18 hr. It is particularly interesting that this structure is so stable under these conditions, since dehydration and rearrangement of the alcohol (10) occurs in the presence of toluene-*p*-sulphonic acid and acetic anhydride.

In view of the postulated role of the $\Delta^{9(11)}$-bond in the



SCHEME 1



SCHEME 2

reactions giving intractable products, two main components were isolated by t.l.c. Each zone appeared to be a mixture of Δ^4- and $\Delta^{4,6}$-3-ketones by u.v. spectroscopy, indicating possible addition of hydrogen chloride,[18] although n.m.r. spectra confirmed the presence of the $\Delta^{4,6,9(11)}$-olefinic proton system. The absence of hydroxy-absorption suggested that partial rearrangement could have occurred, but the components could not be separated.

Further dehydrogenation of the trienone (10) to the tetraenone (4) was accomplished using the standard uncatalysed dichlorodicyanobenzoquinone procedure. This compound (4) was completely stable under normal conditions of manipulation, in marked contrast to the above mechanism, the behaviour of the corresponding compounds lacking this double bond have been examined. The $\Delta^{1,4,6}$-trien-3-one (12), obtained by dehydrogenation of the Δ^5-3-ol (13) with dichlorodicyanobenzoquinone,[19] gave the 7-acetoxytetrahydrophenanthrene (14) in good yield using the standard conditions for dienone–phenol rearrangement. The *gem*-dimethyl groups at C-17 of the acetate (14) resonate at τ 9·10 and 8·91. No Δ^{16}-intermediate was isolated under these conditions, nor in refluxing benzene, although t.l.c. revealed the presence of several mobile products in the

[18] *Cf.* P. A. Diassi, S. D. Levine, and R. M. Palmere, *J. Medicin. Chem.*, 1967, **10**, 551.
[19] A. B. Turner, *J. Chem. Soc.* (*C*), 1968, 2568.

latter reaction. In one case of rearrangement of such a system, pregna-1,4,6,16-tetraene-3,20-dione aromatises only in ring A,[20] and the Δ^{16}-bond does not migrate, although this is probably due to its being in conjugation with the 20-keto-group.

The naphthalene (14) is oxidised by dichlorodicyanobenzoquinone at room temperature to give a mixture of the phenanthrene (6) and its Δ^{15}-derivative (16). The n.m.r. of the latter showed the *gem*-dimethyl group at C-17 as a singlet, and the C-16-proton as a doublet (τ 3·35). The C-15-proton appears downfield in the aromatic proton region. It is noteworthy that the phenanthrene (5) is not dehydrogenated by the quinone to give the Δ^{15}-derivative, either at room temperature or on warming the solution. This clearly shows that the phenanthrene (6) is not an intermediate in the formation of the cyclopentadieno-phenanthrene (16) from the naphthalene (14). Formation of the Δ^{15}-derivative (16) is rationalised by initial hydride abstraction from the tertiary benzylic 14α-position (*cf.* ref. 1) leading to both Δ^{13}- and Δ^{14}-dehydro-derivatives. The former would be oxidised to the phenanthrene (6), whereas the latter could give rise to the Δ^{15}-phenanthrene (16), by the mechanisms outlined in Scheme 2.

EXPERIMENTAL

Steroid nomenclature has been adopted for consistency throughout this section; hence the phenanthrenes appear as gonane derivatives rather than as cyclopenta[*a*]phenanthrenes.

Reagents and solvents were purified as described in previous Parts of this series. I.r. spectra were determined in potassium bromide discs on a Perkin-Elmer 237 Spectrophotometer. Mass spectra were obtained using an AEI MS9 instrument; ions of relative intensity >10% are included. N.m.r. spectra were recorded at 60 MHz in $CDCl_3$ on a Varian A-60 spectrometer, and optical rotations were determined for 2% chloroform solutions at 25° using a Bendix NPL Automatic Polarimeter 143C. Alumina used for column chromatography was Woelm, activity grade I. T.l.c. was performed on silica gel (Merck GF254), using hexane–ethyl methyl ketone (3 : 1) for development, unless otherwise stated.

17β-*Hydroxy*-17α-*methylandrosta*-1,4,9(11)-*trien*-3-*one* (3).—A solution of 17β-hydroxy-17α-methyl-androsta-4,9(11)-dien-3-one (5·0 g.) and dichlorodicyanobenzoquinone (4·92 g., 1·3 equiv.) in dioxan (125 ml.) was heated under reflux for 24 hr. After removal of hydroquinone, the filtrate was evaporated and the residue was dissolved in ether (100 ml.), washed with 2% aqueous sodium hydroxide (3 × 30 ml.), and dried ($MgSO_4$). The crude product left after evaporation of the ether was taken up in benzene and chromatographed on alumina (300 g.). Elution with benzene–ethyl acetate gave the trienone (4·2 g., 85%), which was crystallised from ether–hexane, m.p. 143—145° (lit.,[7,8] 136—139°), $[\alpha]_D = -82·5°$, τ 9·11 (s, 13-Me), 8·81 (s, 17α-Me), 8·57 (s, 10-Me), 4·33 (m, 11-olefinic H), 3·95 (m, 4-olefinic H), 3·67 (dd, *J* 10 and 2 Hz, 2-olefinic H), and 2·72 (d, *J* 10 Hz, 1-olefinic H).

Dehydration of 17β-*Hydroxy*-17α-*methylandrosta*-1,4,9(11)-*trien*-3-*one* (3).—A solution of the above trienone (1·0 g.), the quinone (1·53 g.), and toluene-*p*-sulphonic acid (0·62 g.) in dioxan (30 ml.) was heated for 24 hr. under reflux. Filtration of the cooled mixture gave the hydroquinone (72%). The filtrate was evaporated and the resulting black tar was dissolved in benzene and chromatographed on silica gel (150 g.). Elution with benzene–ethyl acetate (98 : 2) gave a brown oil (586 mg.), which was further purified by t.l.c. Extraction of the major band without delay gave the unstable 17-methylandrosta-1,4,6,9(11),16-pentaen-3-one (7) as a colourless oil (350 mg.), $\lambda_{max.}$ 242 (ε 12,700), 260 (10,400), and 303 nm. (7600); τ 9·20 (s, 13-Me), 8·58 (s, 10-Me), 8·34 (d, *J* 2 Hz, 17-Me), 4·65 (m, 16-olefinic H), 4·40 (m, 11-olefinic H), 3·95—3·55 (m, 2,4,6 and 7-olefinic H), and 2·80 (d, *J* 10 Hz, 1-olefinic H).

Similar treatment of the trienone (200 mg.) in benzene (10 ml.) with toluene-*p*-sulphonic acid (156 mg.) alone, using a water separator, yielded a black solution which was filtered through alumina to give a brown oil (130 mg.). Further purification by t.l.c. gave 17-methylandrosta-1,4,9(11),16-tetraen-3-one as a colourless oil (74 mg.), which could not be crystallised, τ 9·21 (s 13-Me), 8·58 (s, 10-Me), 8·32 (broad s, 17-Me), 4·65 (m, 16-olefinic H), 4·39 (m, 11-olefinic H), 3·88—3·22, and 2·85—2·52 (m, ring A olefinic H's).

3-*Acetoxy*-1,17,17-*trimethylgona*-1,3,5(10),6,8,11,13-*heptaene* (6).—(a) *From* 17-*methylandrosta*-1,4,6,9(11),16-*pentaen*-3-*one* (7). A solution of the freshly purified pentaenone (300 mg.) and toluene-*p*-sulphonic acid (100 mg.) in acetic anhydride (15 ml.) was heated on the steam-bath for 5 hr. The mixture was poured into water (100 ml.) and left overnight before being extracted with ether (3 × 30 ml.). The ethereal extracts were washed with aqueous sodium hydrogen carbonate, dried ($MgSO_4$), and evaporated. T.l.c. of the residue (250 mg.), followed by crystallisation from acetone–hexane, gave the *heptaene* (100 mg., 29%), m.p. 75—76° (Found: C, 82·8; H, 6·8. $C_{22}H_{22}O_2$ requires C, 83·0; H, 6·9%), $[\alpha]_D = 0°$, $\lambda_{max.}$ 260 (ε 73,300), 285 (14,770), 295 (11,730), 307 (9900), and 325 nm. (1520), $\nu_{max.}$ 1775, 1620, 1380, 1245, 1220, 1030, 920, and 820 cm.$^{-1}$; τ 8·65 (s, 17-*gem*-di-Me), 7·66 (s, 3-OAc), 6·90 (s, 1-Me), 7·95 and 6·73 (m, 15- and 16-methylenes), 2·80—2·30 (m, 2,4,6,7 and 12-ArH), and 1·33 (d, *J* 8·5 Hz, 11-ArH).

(b) *From the phenol* (5). A solution of the phenol (100 mg.) in acetic anhydride (5·0 ml.) and pyridine (2·5 ml.) was set aside overnight at room temperature. The usual work-up procedure gave the *acetate* (80 mg., 69%), m.p. 75—76°, identical (i.r. and mixed m.p.) with material obtained by method (a).

(c) *From* 17β-*hydroxy*-17α-*methylandrosta*-1,4,6,9(11)-*tetraen*-3-*one* (4). Dienone–phenol rearrangement of the tetraenone (250 mg.) with toluene-*p*-sulphonic acid was carried out in acetic anhydride as described above. A sample of the crude product (120 mg.) was separated into two components (ratio 3 : 1) by multiple development t.l.c. in ether–hexane (5 : 95). The major product was the more mobile *heptaene* (6), identical to material prepared by method (a), while the more polar hexaene (9) was obtained as a colourless oil (Found: M^+, 320·1769. $C_{22}H_{24}O_2$ requires 320·1776), *m/e* 320 (62%), 278 (53%, $M - CH_2CO$), 264 (18%), 263 (27%), 223 (27%), 222 (100%, $M - C_2H_2O$–C_8H_8), 221 (20%), 209 (32%), 208 (33%), and 207 (20%).

(d) *From* 3-*Acetoxy*-1,17,17-*trimethylgona*-1,3,5(10),6,8-*pentaene* (14).—Solutions of the pentaene (100 mg.) in

[20] C. Djerassi, G. Rosenkranz, J. Iriarte, J. Berlin, and J. Romo, *J. Amer. Chem. Soc.*, 1951, **73**, 1523.

dioxan (3·0 ml.) and dichlorodicyanobenzoquinone (70·5 mg.) in dioxan (2·0 ml.) were mixed and left for 24 hr. at room temperature. The mixture was initially dark green, and the hydroquinone was precipitated after 10 min. The hydroquinone (69 mg.) was collected, and the filtrate yielded a yellow oil (68 mg.) after column chromatography on silica gel. T.l.c. of the oil showed starting material and several products. It was dissolved in dioxan (3·0 ml.) and again treated with the quinone (50 mg.) in dioxan (2·0 ml.). After 24 hr., the hydroquinone (47 mg.) was removed and the residue left after evaporation of the filtrate was purified by t.l.c. to give a colourless oil (58 mg.) which could not be crystallised. Multiple development t.l.c. in hexane–ethyl methyl ketone (95 : 5) separated this oil into two components, the more mobile one being the *heptaene* (32 mg., 32%), identical to material prepared by method (a).

The more polar component (16 mg., 16%) was crystallised from acetone to give 3-acetoxy-1,17,17-trimethylgona-1,3,5(10),6,8,11,13,15-octaene (16), m.p. 121—122°, $\lambda_{max.}$ 263 (ε 44,400), 297 (10,400), 310 (13,300), 322 (12,700), 348 (2300), and 365 nm. (2300); $\nu_{max.}$ 1770 and 1230 cm.$^{-1}$; τ 8·58 (s, 17-*gem*-di-Me), 7·62 (s, 3-OAc), 6·85 (s, 1-Me), 3·35 (d, *J* 6 Hz, 16-olefinic H), 2·80—1·20 (m, olefinic and ArH); *m/e* 316 (44%, $M^{+\cdot}$), 275 (23%), 274 (100%, $M - CH_2CO$), 259 (29%), 244 (15%), and 215 (15%).

3-*Hydroxy*-1,17,17-*trimethylgona*-1,3,5(10),6,8,11,13-*heptaene* (5).—(a) *From the pentaenone* (7). A solution of the freshly purified pentaenone (300 mg.) in ethyl acetate (20 ml.) was boiled with a little activated charcoal for 10 min., and left for 5 days. The charcoal was filtered off and the residue left after evaporation of the filtrate was purified by t.l.c. to give the *heptaene* (5) as a colourless solid (198 mg.), which was crystallised from hexane to m.p. 142—144° (lit.,[11] 144—145°), (Found: C, 86·7; H, 7·3%; *M*$^+$, 276·1521. Calc. for $C_{20}H_{20}O$: C, 86·9; H, 7·3%; *M*, 276·1514), $\lambda_{max.}$ 263 (ε 68,000), 285 (12,200), 195 (10,300), 306 (8800), 344 (1300), and 362 nm. (1300); $\nu_{max.}$ 3320, 1620, 1000, 865, and 815 cm.$^{-1}$; τ 8·65 (s, 17-*gem*-di-Me), 6·98 (s, 1-Me), 7·93 and 6·75 (m, 15 and 16-CH_2), 2·97—2·37 (m, 2-, 4-, 6-, 7-, 12-ArH), 1·33 (d, *J* 8·5 Hz, 11-ArH); *m/e* 276 (45%, $M^{+\cdot}$), 262 (36%), 261 (100%, $M - CH_3$), 247 (50%), 246 (16%), 232 (15%), 231 (25%), 215 (12%), 176 (14%), 138 (M^{2+}, 3%), 130·5 (12%, 261^{2+}), and 123·5 (6%, 247^{2+}).

(b) *From the trienone* (3). A solution of the trienone (500 mg.), the quinone (762 mg., 2 equiv.) and toluene-*p*-sulphonic acid (320 mg.) in dioxan (30 ml.) was heated under reflux for 72 hr. The hydroquinone (68%) was filtered off, and black tar left after evaporation of the filtrate was dissolved in benzene and chromatographed on silica gel (100 g.). Elution with benzene–hexane gave a yellow oil (242 mg., 52%) which was crystallised from hexane to give the *phenol* (5), identical with material prepared by method (a).

(c) *From the acetate* (6). A solution of the acetate (100 mg.) in 4% methanolic sodium hydroxide (50 ml.) was heated under reflux for 4 hr. The usual isolation procedure, followed by crystallisation from hexane, gave the phenol (81 mg., 93%), m.p. 142—153°, identical with material obtained by method (a).

17β-*Hydroxy*-17α-*methylandrosta*-4,6,9(11)-*trien*-3-*one* (10).—(*a*) Dry hydrogen chloride was bubbled into a solution of 17β-hydroxy-17α-methylandrosta-4,9(11)-dien-3-one (5·0 g.) and dichlorodicyanobenzoquinone (4·0 g.) in dry benzene (30 ml.) and dioxan (30 ml.) for 20 sec. The mixture was left at room temperature for 2 hr. before the precipitated hydroquinone (3·5 g.) was collected. The residue left after evaporation of the filtrate was dissolved in 1 : 1 ether–ethyl acetate (100 ml.), washed with 2% aqueous sodium hydroxide (3 × 30 ml.) and then with water, and was then dried ($MgSO_4$). Evaporation gave the crude product (4·3 g.), which contained *ca.* 10% of starting material (estimated by n.m.r. and u.v. spectroscopy). A sample of this material was purified by t.l.c. using benzene–ethyl acetate (4 : 1) as solvent. Removal of the lower half of the main band gave, after extraction and crystallisation from acetone, the *trienone* (10), m.p. 151—153°, $[\alpha]_D$ −110° (Found: C, 80·3; H, 8·7. $C_{20}H_{26}O_2$ requires C, 80·5; H, 8·7%), $\lambda_{max.}$ 284 nm. (ε 20,100); $\nu_{max.}$ 3440 and 1650 cm.$^{-1}$; τ 9·07 (s, 13-Me), 8·77 (s, 17α-Me), 8·68 (s, 10-Me), 4·40 (m, 11-olefinic H), 4·30 (s, olefinic H), and 3·95 (s, 6- and 7-olefinic H).

(*b*) A solution of the 4,9(11)-dien-3-one (2·0 g.) and chloranil (1·83 g.) in t-butyl alcohol (36 ml.) was heated for 30 min. under reflux. The solvent was evaporated *in vacuo* and the residue, in 1 : 1 ether–ethyl acetate (50 ml.), was washed with a 2% aqueous solution of sodium hydroxide (5 × 20 ml.); the solution was then dried ($MgSO_4$). Evaporation of the solvent gave a brown oil which was chromatographed on silica gel (100 g.). Elution with benzene–chloroform gave the trienone (1·09 g.), which was crystallised from acetone, m.p. 148—150° (0·88 g., 44%), undepressed by admixture with material prepared by method (*a*).

17β-*Hydroxy*-17α-*methylandrosta*-1,4,6,9(11)-*tetraen*-3-*one* (4).—A solution of the above 4,6,9(11)-trien-3-one (4·4 g.) and dichlorodicyanobenzoquinone (4·0 g.) in dioxan (80 ml.) was heated under reflux for 24 hr. The hydroquinone (3·5 g.) was removed and the oily residue left after evaporation of the solvent was dissolved in 1 : 1 ether–ethyl acetate (100 ml.); the solution was washed with 2% aqueous sodium hydroxide (3 × 30 ml.), and dried ($MgSO_4$). Evaporation gave a yellow oil which was chromatographed on silica gel (100 g.). Elution with benzene–chloroform gave the crude product (3·7 g., 85%) which was crystallised from acetone to give the *tetraenone*, m.p. 170—171°, $[\alpha]_D$ −239° (Found: C, 79·1; H, 8·3. $C_{20}H_{24}O_2,\frac{1}{2}C_3H_6O$ requires C, 79·4; H, 8·3%), $\lambda_{max.}$ 232 (ε 11,700), 253 (9400), and 299 nm. (10,000); $\nu_{max.}$ 3400, 1670, 1615, and 900 cm.$^{-1}$; τ 9·05 (s, 13-Me), 8·80 (s, 17α-Me), 8·58 (s, 10-Me), 7·84 (s, 3H, ½ acetone solvate), 4·38 (m, 11-olefinic H), 4·08—3·58 (m, 2-, 4-, 6-, and 7-olefinic H), and 2·82 (d, *J* 10 Hz, 1-olefinic H). This compound was also obtained as an ether solvate from ether–hexane, m.p. 77—80°, resolidifying, then m.p. 161—164°.

The acetate of this alcohol was prepared by heating a sample (132 mg.) in acetic anhydride (10 ml.) under reflux for 18 hr. The usual work-up procedure gave 17β-*acetoxy*-17α-*methylandrosta*-1,4,6,9(11)-*tetraen*-3-*one* (102 mg., 66%), m.p. 214—215° (from acetone) (Found: C, 77·8; H, 7·8. $C_{22}H_{26}O_3$ requires C, 78·1; H, 7·7%), $\lambda_{max.}$ 231 (ε 13,200), 253 (10,600), and 298 nm. (9900); $\nu_{max.}$ 1730, 1665, and 1255 cm.$^{-1}$; τ 9·09 (s, 13-Me), 8·61 (s, 17α-Me), 8·58 (s, 10-Me), 8·00 (s, 17β-OAc), 4·38 (m, 11-olefinic H), 4·08—3·58 (m, 2-, 4-, 6-, and 7-olefinic H), and 2·82 (d, *J* 10 Hz, 1-olefinic H).

17β-*Hydroxy*-17α-*methylandrosta*-1,4,6-*trien*-3-*one* (12).—A solution of 3β,17β-dihydroxy-17α-methylandrost-5-ene (2·0 g.) and dichlorodicyanobenzoquinone (4·9 g., 3·3 equiv.) in dioxan (50 ml.) was heated for 24 hr. under reflux. The hydroquinone (4·1 g.) was removed and the brown oil left after evaporation of the dioxan was taken up in 1 : 1 ether–ethyl acetate; the solution was washed with 2% aqueous

sodium hydroxide (3 × 30 ml.), dried ($MgSO_4$), and evaporated. The residual yellow oil was chromatographed on silica gel to give the trienone (1·12 g., 57%), m.p. 131—134° (from acetone–hexane), raised upon recrystallisation from acetone to 136—138° (lit.,[21] 139—140°); τ 9·02 (s, 13-Me), 8·77 (s, coincident 17α- and 10-Me), 4·03—3·58 (m, 2-, 4-, 6-, and 7-olefinic H), and 2·90 (d, *J* 10 Hz, 1-olefinic H).

3-*Acetoxy*-1,17,17-*trimethyl*-13ξ,14ξ-*gona*-1,3,5(10),6,8-*pentaene* (14).—A solution of the above 1,4,6-trien-3-one (1·0 g.) and toluene-*p*-sulphonic acid (0·64 g.) in acetic anhydride (30 ml.) was heated for 5 hr. on the steam-bath. The cooled solution was poured into water (200 ml.) and left for 12 hr. before the oily precipitate was extracted into ether (3 × 30 ml.). The extract, after being washed with sodium hydrogen carbonate and water, was dried and evaporated. The resulting yellow oil was chromatographed on silica gel (50 g.). Elution with hexane–benzene gave the naphthalene as a colourless oil (0·74 g.), which crystallised from hexane, m.p. 73—74° (lit.,[11] 82—83·5°), (Found: C, 81·7; H, 8·2. Calc. for $C_{22}H_{26}O_2$: C, 81·9; H, 8·2%), $\lambda_{max.}$ 235 (ε 70,500), 260 (13,300), 285 (7350), 295 (5980), and 316 nm. (1380); $\nu_{max.}$ 1750, 1220, and 1210 cm.$^{-1}$; τ 9·10 and 8·91 (s, 17α- and 17β-Me), 7·71 (s, 3-OAc), 7·10 (s, 1-Me), 3·10—2·35 (m, 2-, 4-, 6-, and 7-ArH).

This acetate (200 mg.) was hydrolysed by heating it under reflux for 2 hr. with 5% methanolic potassium hydroxide (20 ml.). The crude product, obtained by extraction of the acidified solution with ether, was chromatographed on silica gel (20 g.). Eluted with hexane–benzene, the 3-hydroxy-1,17,17-trimethyl-13ξ,14ξ-gona-1,3,5(10),6,8-pentaene (174 mg.) was crystallised from hexane to m.p. 158—160° (lit.,[11] 163·5—164°) (Found: C, 85·4; H, 8·9. Calc. for $C_{20}H_{24}O$: C, 85·7; H, 8·6%), $\lambda_{max.}$ (ε 56,500), 263 (12,500), 283 (8500), 294 (6250), and 307 nm. (2500); $\nu_{max.}$ 3200 cm.$^{-1}$; τ 9·10 and 8·91 (s, 17α- and 17β-Me), 7·12 (s, 1-Me), 3·2—2·25 (m, 2-, 4-, 6-, and 7-ArH).

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