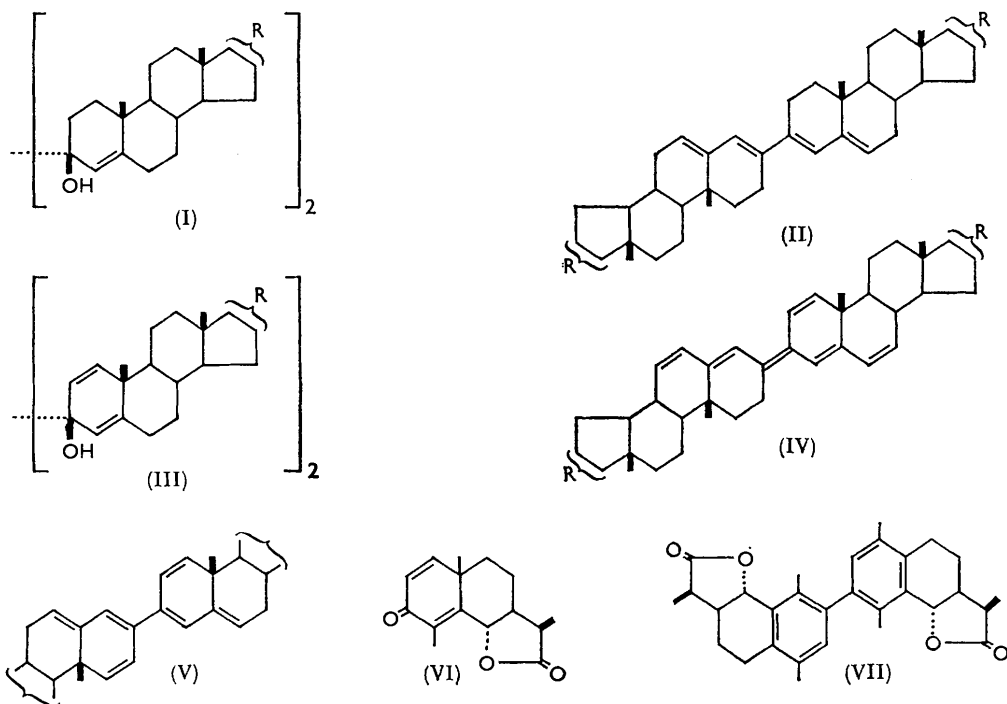


453. The Electrolytic Reduction of Unsaturated Steroid Ketones.
Part II.¹ The Structures of Some Steroid Polyenes.

By PETER BLADON and JAMES REDPATH.

Electrolytic reduction of unsaturated 3-oxo-steroids leads to the formation of pinacols. The structures of the polyolefins formed by dehydration of the pinacols are discussed.

IN Part I of this series¹ was described the electrolytic reduction of cholest-4-en-3-one to yield the pinacol (I; R = 17 β -C₈H₁₇). In order to test the general applicability of this reaction, a number of steroid ketones, including examples of Δ^4 -, $\Delta^{4,6}$ -, $\Delta^{4,7}$ -, and $\Delta^{1,4}$ -unsaturated 3-ketones, were reduced electrolytically by essentially the same method. Each gave a pinacol, which, by analogy with that formed from cholest-4-en-3-one, is assumed to have the 3 β -hydroxyl configuration. The full range of compounds tested is listed in Table I.



Cholestenone pinacol (I; R = 17 β -C₈H₁₇) is known² to be readily dehydrated to bicholesta-3,5-dienyl (II; R = 17 β -C₈H₁₇), and the pinacol (I; R = 16 β ,17 β -C₈H₁₄O₂)

¹ Part I, Bladon, Cornforth, and Jaeger, *J.*, 1958, 863.

² Squire, *J. Amer. Chem. Soc.*, 1951, **73**, 2587.

formed from Δ^4 -tigogenone behaved similarly on treatment with mineral acid, yielding the tetraene (II; R = $16\beta,17\beta\text{-C}_8\text{H}_{14}\text{O}_2$).

On treatment with mineral acid, the pinacol (III; R = $17\beta\text{-C}_8\text{H}_{17}$) derived from cholesta-1,4-dien-3-one yielded a hydrocarbon, m. p. 196° , λ_{max} 242, 360, 378 $\text{m}\mu$ (ϵ 9000, 12,700, 12,500), presumably identical with the hydrocarbon isolated by Kirk, Patel, and Petrow³ on reduction of cholesta-1,4-dien-3-one with zinc and acetic acid. This is assigned structure (IV; R = $17\beta\text{-C}_8\text{H}_{17}$) for the following reasons. The wavelength of maximum ultraviolet absorption is considerably higher than that of bicholesta-3,5-dien-3-yl (see Fig. 1), and the most obvious structure (V), having four linear conjugated double bonds and two cross-conjugated components, would be expected to have light absorption roughly comparable to that of this simple analogue. The bathochromic shift (48 $\text{m}\mu$) can be accounted for by the presence of an additional double bond in linear conjugation,

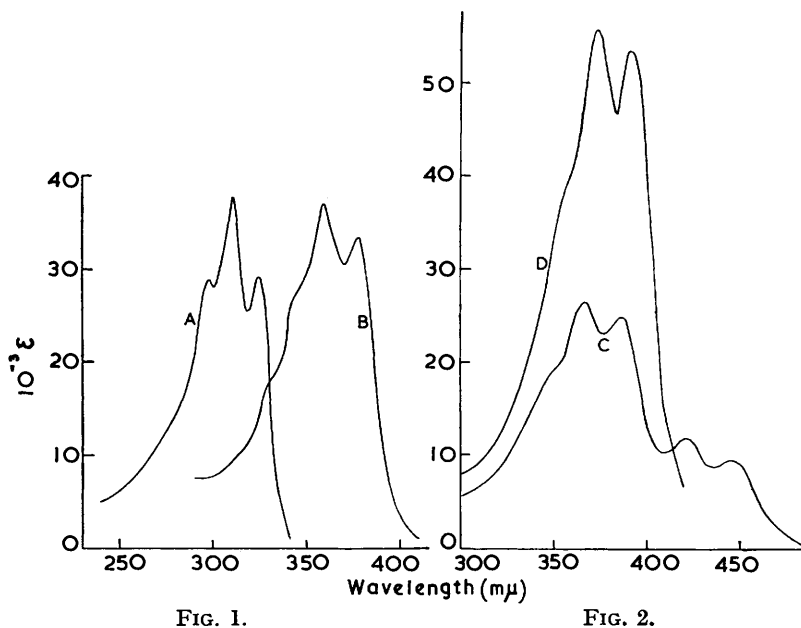


FIG. 1. Light absorption in chloroform of: (A) 3,3'-Bicholesta-3,5-dienyl;¹
(B) 3-(3-cholesta-4,6-dienylidene)cholesta-1,4,6-triene.

FIG. 2. Light absorption in chloroform of: (C) 3,3'-bi ergosta-3,5,7,22-tetraen-3-yl;
(D) 3-(3'-cholesta-4',6'-dienylidene)cholesta-4,6,8(14)-triene.

as in (IV), for which, according to the Woodward-Fieser rules,⁴ the calculated wavelength of maximum light-absorption is 355 $\text{m}\mu$ (when the effect of the cross-conjugated double bond is neglected). A similar dehydration product (IV; R = $16\beta,17\beta\text{-C}_8\text{H}_{14}\text{O}_2$) was formed from the pinacol derived from the sapogenin ketone (III; R = $16\beta,17\beta\text{-C}_8\text{H}_{14}\text{O}_2$).

Reduction of santonin (VI), which has the similar cross-conjugated dienone system, with zinc and acetic acid is reported to give the bimolecular santonone (VII).⁵ The light absorption [λ_{max} (in chloroform) 246, 274 $\text{m}\mu$ (ϵ 7624, 3015) (hitherto unreported)] is consistent with an aromatized structure but is different from that of 2,2'-dimethylbiphenyl⁶

³ Kirk, Patel, and Petrow, *J.*, 1957, 1046.

⁴ Fieser and Fieser, "Steroids," Reinhold Publ. Inc., New York, 1959, p. 17.

⁵ Simonsen, "The Terpenes," Cambridge Univ. Press, Cambridge, 1952, Vol. III, p. 274; Pannain, *Atti Accad. naz. Lincei, Rend. Classe Sci. Fis. mat. nat.*, 1908, **17**, 499; *Gazzetta*, 1909, **39**, 515.

⁶ O'Shaughnessy and Rodebush, *J. Amer. Chem. Soc.*, 1940, **62**, 2906; Braude and Waight in "Progress in Stereochemistry," ed. Klyne, Butterworths Scientific Publins., London, Vol. I, 1954, p. 441.

TABLE I.
Pinacols.

Ref.*	Pinacol	M. p.	$[\alpha]_D$	λ_{max}^e (m μ)	ϵ	Found (%) C H	Formula	Required (%) C H
12	3,3'-Bi-(25d, 3 β -hydroxy Spirost-4-enyl) (I; R = 16 β ,17 β -C ₈ H ₁₄ O ₂)	280 ^a	-56.1°	206	10,400	78.1 10.0	C ₅₄ H ₈₈ O ₄	78.3 9.95
13	3,3'-Bi-(3 β -hydroxycholesta-1,4-dienyl) (II; R = 17 β -C ₈ H ₁₄ O ₂)	130 ^{a,b}	+68.1°	206	17,400	84.2 11.4	C ₅₄ H ₈₈ O ₂	84.5 11.2
14	3,3'-Bi-(25d, 3 β -hydroxy Spirost-1,4-dienyl) (III; R = 16 β ,17 β -C ₈ H ₁₄ O ₂)	250 ^a	-49.7°	206	15,700	79.4 9.4	C ₅₄ H ₇₈ O ₄	78.8 9.5
1	3,3'-Bi-(3 β -hydroxyergosta-4,7,22-trienyl) (VIII)	240 ^c	-11.2°	209	14,400	81.9 10.7	C ₅₄ H ₈₈ O ₂ , 2H ₂ O	81.4 10.9
16	3,3'-Bi-(3 β -hydroxycholesta-4,6-dienyl) (X; R = 17 β -C ₈ H ₁₇)	152°	+36.6°	208	8600	80.8 10.8	C ₅₄ H ₈₈ O ₂ , 2H ₂ O	80.8 11.2
15	3,3'-Bi-(3 β -hydroxyergosta-4,6,22-trienyl) (X; R = 17 β -C ₈ H ₁₇)	180 ^a	-12.1°	236	9100	85.3 11.3	C ₅₄ H ₈₈ O ₂	85.2 11.0
17	3,3'-Bi-(25d, 3 β -hydroxy Spirost-4,6-dienyl) (X; R = 16 β ,17 β -C ₈ H ₁₄ O ₂)	300 ^a	-21.5°	234 208 235	10,900 9000 10,000	78.8 9.5	C ₅₄ H ₇₈ O ₄	78.7 9.8

Footnotes to Table I: ^a From C₈H₁₇-COMe; ^b With decomp. ^c From aq. COMe; ^d In CHCl₃; ^e In EtOH.
^{*} Ref. for starting material: ¹³ Marker, Tsukamoto, and Turner, *J. Amer. Chem. Soc.*, 1940, **62**, 2525. ¹⁴ Butenandt, Mamoli, Dannenberg, Masch, and Paland, *Ber.*, 1939, **72**, 1617 (we thank Dr. A. G. Long, of Glaxo Laboratories, for a sample of cholesta-1,4-dien-3-one). ¹⁵ Miki and Hara, *Pharm. Bull. (Japan)*, 1956, **4**, 421; Burn, Ellis, and Petrov, *J.*, 1958, 795 (our sample was prepared by the method of Burn, Kirk, and Petrov, *Proc. Chem. Soc.*, 1960, 14). ¹⁶ Shepherd, Denta, Campbell, Johnson, Holyez, Slomp, Stafford, Pederson, and Ott, *J. Amer. Chem. Soc.*, 1955, **77**, 1212. ¹⁷ Wettstein, *Helv. Chim. Acta*, 1940, **23**, 388. ¹⁸ Marker and Turner, *J. Amer. Chem. Soc.*, 1941, **63**, 767.

TABLE 2.

Dehydration products of pinacols.

Product	M. p.	$[\alpha]_D$ †	λ_{max}^e (m μ) ‡	ϵ	Crystn. solvent †	Found (%) C H	Formula	Required (%) C H
3,3'-Bi-(25d-spirosta-3,5-dienyl) (II; R = 16 β ,17 β -C ₈ H ₁₄ O ₂)	>360°	-27.5°	300 310 324	31,900 45,700 42,600	CHCl ₃ -MeOH	82.0 9.6	C ₅₄ H ₇₈ O ₄	82.1 9.8
3-(3-Cholesta-4,6-dienylidene)cholesta-1,4,6-triene (IV; R = 17 β -C ₈ H ₁₇) [*]	196	+14.5	3281 358 377	17,500 37,200 33,600	Pet	88.4 11.4	C ₅₄ H ₈₂	88.7 11.3
3-(3-25d-Spirosta-4,6-dienylidene)-25d-spirosta-1,4,6-triene (IV; R = 16 β ,17 β -C ₈ H ₁₄ O ₂)	>360	-47.2	3401 360	15,600 21,400	CHCl ₃ -MeOH	82.1 9.4	C ₅₄ H ₇₄ O ₄	82.4 9.4
3,3'-Bi(ergosta-3,5,7,22-tetraenyl) (IX; R = C ₈ H ₁₇)	234	+44.9	376 3511 366	22,800 19,500 26,300	Pet (chrom)	89.5 10.9	C ₅₄ H ₈₂	89.2 10.8
3-(3-Cholesta-4,6-dienylidene)cholesta-4,6,8-triene (XI; R = 17-C ₈ H ₁₇)	214	+7	374 392	55,600 53,600	Pet (chrom)	88.5 11.4	C ₅₄ H ₈₂	88.7 11.3
3-(3-Ergosta-4,6,22-trienylidene)ergosta-4,6,8,22-tetraene (XI; R = C ₈ H ₁₇)	245	+3	3601 374	41,500 52,400	Pet	89.3 11.0	C ₅₄ H ₈₂	89.2 10.8
3-(3-25d-Spirosta-4,6'-dienylidene)-25d-spirosta-4,6,8-triene (XI; R = 16 β ,17 β -C ₈ H ₁₄ O ₂)	276	-40.5	374 392	45,200 60,600	Pet	82.2 9.4	C ₅₄ H ₇₄ O ₄	82.4 9.4

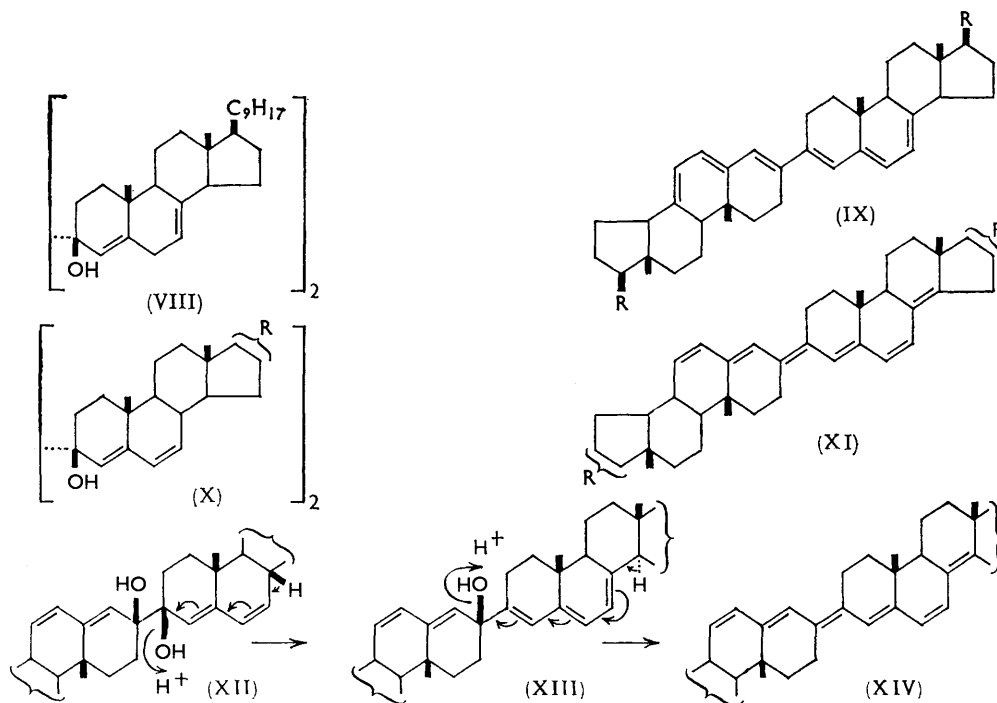
Footnotes to Table 2: ^{*} Kirk *et al.*³ record m. p. 190—196°; λ_{max}^e (in hexane) 250, 336, and 352 m μ ($E_{1\%}^{1\text{cm}}$ 116, 264, 265). † Pet = light petroleum (b. p. 40—60°); chrom = after chromatography. ‡ In CHCl₃; † = inflexion.

which has no maximum above 220 $m\mu$. The behaviour of santonin and the steroid 1,4-dien-3-ones on bimolecular reduction is clearly different, and the structure of santonone is worthy of reinvestigation.

The pinacol (VIII) derived from ergosta-4,7,22-trien-3-one gave, on treatment with mineral acid, the hydrocarbon (IX; $R = C_9H_{17}$) characterised by its high positive optical rotation. The absorption spectrum (see Fig. 2) showed two long-wavelength bands, consistent with the structure's having six linear conjugated double bonds and two homoannular diene moieties; the most intense peak is of lower-wavelength (366 $m\mu$), presumably owing to incomplete conjugation in the chromophore resulting from slight non-coplanarity of the two steroid nuclei.

Surprisingly the pinacol (X; $R = 17\beta-C_9H_{17}$) from ergosta-4,6,22-trien-3-one did not yield the same hydrocarbon on dehydration but an isomer, formulated as the conjugated hexaene (XI; $R = 17\beta-C_9H_{17}$) on account of its absorption spectrum (see Fig. 2 for the spectrum of the analogous cholestane derivative). The long-wavelength peak occurs at 392 $m\mu$, the calculated⁴ value being 405 $m\mu$. In this case the dehydration must proceed in the manner indicated (XII \rightarrow XIII \rightarrow XIV).

Bergmann and Ottke,⁷ and Arima and Hayatsu⁸ have reported the formation of a bicholestatrienyl as a by-product in application of the bromination-dehydrobromination⁹



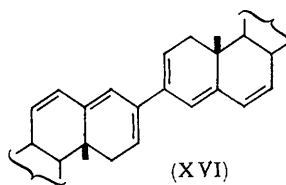
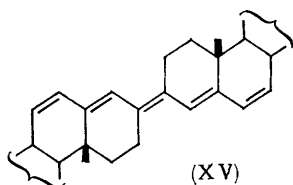
reaction to cholesteryl esters and this was assigned¹⁰ the structure (IX; $R = C_8H_{17}$). The high negative rotation ($[\alpha]_D -200^\circ$) and absorption spectrum (λ_{max} 352, 369.5 $m\mu$; ϵ 33,500, 36,500) are in contrast to the properties of the biergosta-3,5,7,22-tetraen-3-yl (IX; $R = C_9H_{17}$) described above. In fact, the light absorption, being very similar to that of the compound (IV) described above, is more in line with the structure (XV).

⁷ Ottke and Bergmann, *Nature*, 1950, **166**, 997; cf. Hafez, *Nature*, 1950, **165**, 401.

⁸ Arima and Hayatsu, *Pharm. Bull. (Japan)*, 1953, **1**, 212.

⁹ Bernstein, Binovi, Dorfman, Sax, and Subbarow, *J. Org. Chem.*, 1949, **14**, 433.

¹⁰ Arima and Hayatsu, *Pharm. Bull. (Japan)*, 1953, **1**, 216; Arima, *ibid.*, p. 220.



Structure (XV) has one less double bond than (IX) and requires a molecular formula $C_{54}H_{84}$; the analyses are insensitive to the two hydrogen atoms.

A second bicholestatrienyl (" bicholestatriene C ") described by Arima,¹¹ [m. p. 240—245° (decomp.); λ_{max} . (in cyclohexane) 307, 320, 379, 394 $m\mu$ (ϵ 9900, 13,800, 25,100, 27,500)] and assigned the $\Delta^{2,4,6}$ -structure (XVI) by him, is possibly the *cis*-isomer of the hydrocarbon (XI; R = C_8H_{17}).

EXPERIMENTAL

Electrolytic Reduction of the Ketones.—The ketone (1—6 g.) in ethanol (750 ml.) containing hydrated sodium acetate (12 g.) was electrolysed as described¹ for cholest-4-en-3-one. The solution was poured into water (3 l.) and extracted with benzene. Drying (Na_2SO_4) of the extract and evaporation afforded the crude pinacol which was recrystallised or in some cases chromatographed on alumina. In the latter cases the pinacols were usually eluted with ether or ether-methanol. The *products* are reported in Table 1.

Dehydration of Pinacols by Acid.—The pinacol (0.5—1 g.) in chloroform (10—50 ml.) and methanol (5 ml.) was treated with concentrated hydrochloric acid (several drops to 1 ml.). The mixture was left with occasional shaking for 24 hr. or refluxed for 1 hr. The solution was washed with aqueous sodium hydrogen carbonate, dried (Na_2SO_4), and evaporated. In all cases, save two, the dehydration product was purified by direct crystallisation. Details of the *products* are given in Table 2.

The authors are indebted to Mr. Wm. McCorkindale for microanalyses.

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¹¹ Arima, *Pharm. Bull. (Japan)*, 1953, **1**, 224.