A Note on the Constitution of Dehydroergopinacone.

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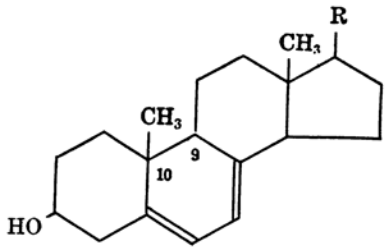
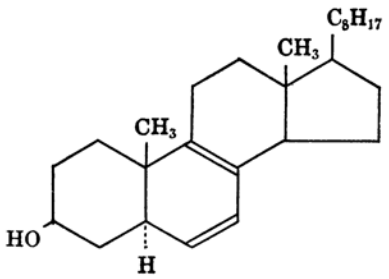
Since ergosterol (Ia) was found to be transformed into a dimolecular dehydrogenation product $C_{56}H_{86}O_2$, the so-called ergopinacone, on exposing it to sunlight with eosin in alcoholic solution in the absence of oxygen[1], some analogously constructed sterol derivatives, e.g. 22-dihydroergosterol (Ib)[2], 7-dehydrocholesterol (Ic)[3][4], and 7-dehydrositosterol (Id)[5], have been shown to undergo similar dehydrogenation. The location of the conjugate double bonds at the same positions as in ergosterol seems however neither necessary nor sufficient for the pinacone formation, because, on the one hand, Windaus and Zühlsdorff[6] obtained the same product from $\Delta^{6,8}$-cholestadienol (II) and from $\Delta^{6,8}$-coprostadienol (III) as from 7-dehydrocholesterol (Ic), and, on the other, of the four stereoisomerides, ergosterol, lumisterol, pyrocalciferol, and isopyrocalciferol, represented by formula Ia, in which the stereovariants are the carbon atoms 9 and 10[7], ergosterol and pyrocalciferol (acetate)[7] yield "pinacones", while lumisterol[8] and isopyrocalciferol (acetate)[7] do not. An additional double bond between the carbon atoms 9 and 11 facilitates the pinacone formation. Thus dehydroergosterol (IV)[9] derived from ergosterol or isopyrocalciferol, and dehydrolumisterol (V) (acetate)[8] from lumisterol and pyrocalciferol, are both able to form "pinacones" more easily than ergosterol. Thus Kennedy and Spring[7] inferred that the pinacone formation depends on the absence of the steric effect of

(1) A. Windaus and P. Borgeaud, *Ann.*, **460** (1928), 235.
(2) A. Windaus and R. Langer, *ibid.*, **508** (1933), 105.
(3) Y. Urushibara and T. Ando, this Bulletin, **11** (1936), 802; **12** (1937), 495; T. Ando, *ibid.*, **14** (1939), 285.
(4) F. Schenck, K. Buchholz, and O. Wiese, *Ber.*, **69** (1936), 2696.
(5) W. Wunderlich, *Z. physiol. Chem.*, **241** (1936), 116.
(6) A. Windaus and G. Zühlsdorff, *Ann.*, **536** (1938), 204.
(7) T. Kennedy and F. S. Spring, *J. Chem. Soc.*, **1939**, 250.
(8) K. Dimroth, *Ber.*, **69** (1936), 1123.
(9) A. Windaus and O. Linsert, *Ann.*, **465** (1928), 148.

the C_9-hydrogen on the C_{10}-methyl group and concluded that the C_{10}-methyl group and the C_9-hydrogen atom are cis-oriented in lumisterol and isopyrocalciferol and trans-oriented in ergosterol and pyrocalciferol. Such structural characteristics of steroids capable of pinacone formation seem to afford little bases for the consideration of the constitution of "pinacones".



(Ia) R = C_9H_{17}
(Ib) R = C_9H_{19}
(Ic) R = C_8H_{17}
(Id) R = $C_{10}H_{21}$



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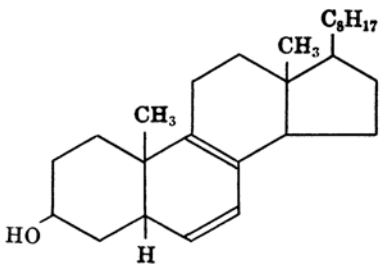
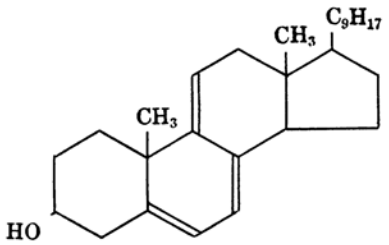


(III)



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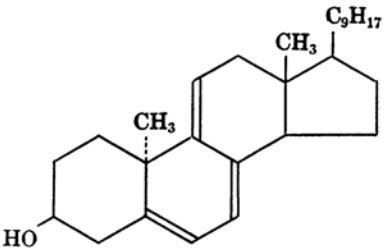

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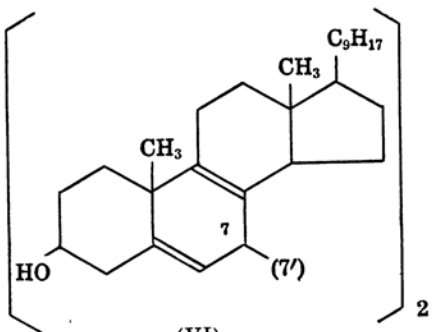
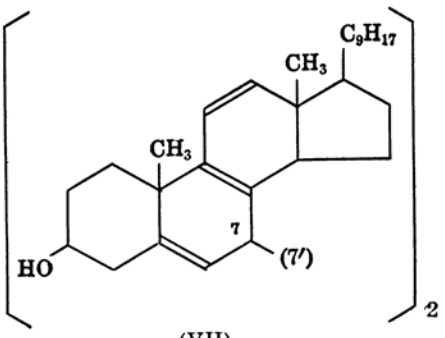


(VI)



(VII)

It has already been shown from various sides that the so-called pinacones are by no means real pinacones, but di-secondary dihydric alcohols, and thus it is very probable that the carbon atom 3 or the hydroxyl group there does not take part in the pinacone formation. The preparation of a similar dehydrogenation product from 7-dehydrocholestene in this laboratory[10] confirms this view conclusively.

Inhoffen[11] presented a tentative formula (VI) for ergopinacone. The isolation by the present author[12] of iso-dehydroergosterol $C_{28}H_{42}O$ besides neoergosterol[1][13] from the pyrolysis of ergopinacone has substantiated Inhoffen's hypothetical formulation[11] for the decomposition of ergopinacone. Inhoffen's formula is well consistent also with the fact that "pinacones" show no longer the absorption spectrum of ergosterol[14][15].

In an attempted dehydrogenation of ergopinacone diacetate with mercuric acetate according to the method of preparation of dehydroergosterol from ergosterol, the starting material was recovered unchanged. This finding may be regarded as another indication that the original conjugate double bonds in ergosterol are not retained in ergopinacone.

The author has examined the absorption spectra of dehydroergopinacone to see if there remain any conjugate double bonds in this "pinacone". On account of the small solubility of dehydroergopinacone, its diacetate was derived from the former in the usual way. Dehydroergopinacone diacetate thus prepared forms needles melting at 195–196.5° (corr.) to an opaque yellow mass and clearing with decomposition at 200.5° (corr.), gives a specific rotation $[\alpha]_D^{32°} = -242°$ in chloroform solution, and shows a characteristic colour change with trichloroacetic acid as described in the experimental part. In hexane solution it shows a distinct absorption band in ultraviolet region with a maximum at 275 mμ ($\log \varepsilon_{max} = 3.8$). Dehydroergopinacone diacetate was prepared also by the photochemical dehydrogenation of dehydroergosteryl acetate. This specimen gave just the same melting point, the same specific rotation, and an identical absorption spectrum as the specimen described above.

Dehydroergosterol shows an absorption maximum at 320 mμ in accordance with the three conjugate double bonds in the molecule. This maximum is no longer present in the absorption spectrum of dehydroergopinacone, but the appearance of a maximum at 275 mμ indicates that two double bonds are conjugated in a ring. If Inhoffen's formula for ergopinacone is followed, formula VII can be given to dehydroergopinacone.

Experimental.

Dehydroergosterol. Prepared from ergosterol (3.00 g.) and mercuric acetate (6.90 g.) in alcoholic solution according to the directions of Windaus and Linsert[9]. On

(10) A. Tominaga, this Bulletin, **14** (1939), 486.
(11) H. H. Inhoffen, *Naturwissenschaften*, **25** (1937), 125.
(12) T. Ando, this Bulletin, **14** (1939), 169.
(13) K. Bonstedt, *Z. physiol. Chem.*, **185** (1929), 165; H. H. Inhoffen, *Ann.*, **497** (1932), 130; H. Honigmann, *ibid.*, **511** (1934), 292.
(14) T. Ando, this Bulletin, **14** (1939), 285.
(15) K. Buchholz, Inaugural Dissertation, Göttingen, 1937.

recrystallizing repeatedly from chloroform-methanol and then from 80% alcohol dehydroergosterol formed colourless small plates (1.05 g.), m.p. 146–147° (corr.).

Acetate. Prepared from dehydroergosterol (365 mg.), acetic anhydride (5.6 g.), and pyridine (3 c.c.). Recrystallization from chloroform-methanol gave colourless plates (337 mg.), m.p. 147.5–148.5° (corr.).

Dehydroergopinacone. Prepared from dehydroergosterol substantially according to the directions of Windaus and Linsert[9]. To remove air, carbon dioxide was passed for thirty minutes through an alcoholic solution (250 c.c. of 95% alcohol) of dehydroergosterol (1.04 g.) and eosin (1.04 g.). After a week's exposure of the solution to sunlight the needles which separated out were collected, washed (ca. 600 mg.), and recrystallized three times from pyridine–95% alcohol. Colourless extremely fine needles (217 mg.), m.p. 198.5–200.5° (corr.).

Acetate. The above dehydroergopinacone (130 mg.) was dissolved in pyridine (20 c.c.) and acetic anhydride (2.0 g.) was added. After standing at room temperature for two days, the orange-red mixture was poured into ice water, and the separating slightly yellowish crystals (130 mg.) were collected after standing overnight, washed with water, with dilute acetic acid, and again with water, recrystallized three times from benzene–95% alcohol, and dried in vacuum at 110° over phosphorus pentoxide. Colourless fine needles (71 mg.), melting at 191–192.5° (uncorr.) or 195–196.5° (corr.) to an opaque yellowish mass and clearing with decomposition at 196.5° (uncorr.) or 200.5° (corr.) to a brownish orange liquid (Found: C, 82.96, 83.10; H, 10.21, 10.02. Calculated for $C_{60}H_{86}O_4$: C, 82.69; H, 9.96 %). $[\alpha]_D^{32°} = -242°$ (11.9 mg. in 1 c.c. chloroform solution, $l = 1$ dm., $\alpha_D^{32°} = -2.88°$). Ultraviolet absorption maximum in 0.048% hexane solution 275 mμ (distinct), $\log \varepsilon_{max} = 3.8$. In the Rosenheim test the diacetate gives pink, light green, green, and finally dark green colouration.

Dehydroergopinacone Diacetate from Dehydroergosteryl Acetate. A solution of dehydroergosteryl acetate (337 mg.) and eosin (337 mg.) in 95% alcohol (100 c.c.) was exposed to sunlight after removing air by passing carbon dioxide. The precipitation appeared to occur sooner in this case. After a week's irradiation the deposit (ca. 140 mg.) was collected, washed, recrystallized four times from benzene–95% alcohol, and dried in vacuum at 110° over phosphorus pentoxide. Colourless fine needles (85 mg.), melting at 191–192.5° (uncorr.) or 195–196.5° (corr.) to an opaque yellowish mass and clearing with decomposition at 197.5° (uncorr.) or 201.5° (corr.) to a brownish orange liquid (Found: C, 82.83; H, 9.98. Calculated for $C_{60}H_{86}O_4$: C, 82.69; H, 9.96%). No depression of the melting point was observed in admixture with the specimen of dehydroergopinacone diacetate prepared from dehydroergopinacone. $[\alpha]_D^{28°} = -242°$ (9.35 mg. in 1 c.c. chloroform solution, $l = 1$ dm., $\alpha_D^{28°} = -2.26°$). Ultraviolet absorption maximum in 0.045% hexane solution 275 mμ (distinct), $\log \varepsilon_{max} = 3.8$.

Attempted Dehydrogenation of Ergopinacone Diacetate with Mercuric Acetate. A mixture of a solution of ergopinacone diacetate[14] (200 mg., m.p. 206.5–207°, $[\alpha]_D^{16°} = -202°$) in benzene (15 c.c.) and a solution of mercuric acetate (480 mg.) in alcohol (10 c.c.) containing a few drops of glacial acetic acid was boiled for two and a half hours. The filtered yellowish solution was evaporated up under diminished pressure, and the residual crystals were dissolved in chloroform. The chloroform solution was filtered to remove insoluble matters, and was again evaporated up. The residue was recrystallized four times from benzene–95% alcohol, and dried in vacuum at 110° over phosphorus pentoxide. Colourless fine needles (135 mg.), m.p. 201.5–202° (uncorr.) or 206–206.5° (corr.) with decomposition. No depression of the melting point was observed in admixture with the specimen of original ergopinacone diacetate, while the melting point was lowered when mixed with dehydroergopinacone diacetate (mixed m.p. 189.5–193.5°, uncorr.). The substance gave an identical specific rotation with ergopinacone diacetate: $[\alpha]_D^{28°} = -202°$ (11.3 mg. in 1 c.c. chloroform solution, $l = 1$ dm., $\alpha_D^{28°} = -2.28°$).

Summary.

Dehydroergopinacone diacetate was prepared and its absorption spectrum in ultraviolet region was studied. Ergopinacone diacetate was shown not to be dehydrogenated with mercuric acetate. From the results a probable constitution (VII) was assigned to dehydroergopinacone, following Inhoffen's ergopinacone formula.

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