699. *Steroids. Part XXII.* The Configuration of 14α-Digiprogenin.*

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The configuration at C-17 of (" γ ")-14α-digiprogenin has been established; this digitenol is 3β,17β-dihydroxy-14α,17α-pregn-5-ene-11,15,20-trione.

THE structure of (" γ ")-14α-digipronin [= Crystal C] (I; R = $C_7H_{12}O_4$), a D(+)-digitaloside isolated from the leaves of *Digitalis purpurea* by Satoh *et al.*[1] and by Tschesche *et al.*,[2] and of its aglycone the digitenol 14α-digiprogenin [= γ-digiprogenin] (I; R = H) have been established by Satoh[3,4] except in regard to configuration at C-17. The 17-side-chain in 14α-digiprogenin (I; R = H) and in 14β-digiprogenin [= α-digiprogenin] (II; R = H) was assigned the β-configuration, and in consequence the tertiary 17-hydroxyl group given the α-orientation, by Satoh[4] simply on the ground of analogy to other natural steroids. We now show that 14α- and 14β-digiprogenin (I and II; R = H) belong to the 17β-hydroxy-17α-pregnan-20-one series.

The conversion of 14α-digipronin into 14β-digipronin (I ⟶ II; R = $C_7H_{12}O_4$) and of 14α-digiprogenin into 14β-digiprogenin (I ⟶ II; R = H) by 0·02N-potassium hydroxide at 20°, and the dehydration of either genin to the 14β-16-en-15-one [= β-digiprogenin] [(I or II; R = H) ⟶ (III)] by N-hydrochloric acid in refluxing 50% ethanol,[3,4] is closely

(I)   (II)   (III)

(IV)   (V)   (VI)
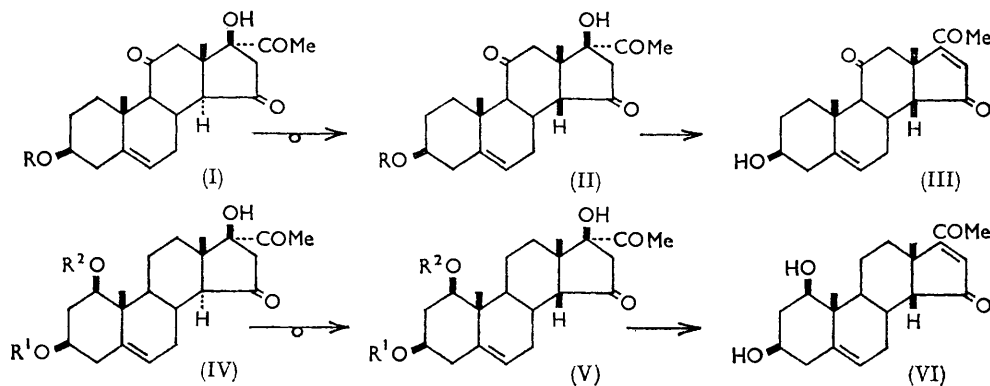
paralleled by the transformation of the tris-D(+)-digitoxoside deacetyl-14α-digacetin to deacetyl-14β-digacetinin (IV ⟶ V; $R^1 = C_{18}H_{30}O_9$, $R^2 = H$) and of deacetyl-14α-digacetigenin to deacetyl-14β-digacetigenin (IV ⟶ V; $R^1 = R^2 = H$) by 0·04N-potassium hydroxide at 20°,[5,6] and the dehydration of the latter genin to the 14β-16-en-15-one (VI) by 2N-hydrochloric acid in refluxing methanol.[6]

The identification by Satoh[3,4] of a 20-methyl-20-carbonyl grouping attached to C-17 in a $>$C(OH)·COMe system, through the characteristic " O "-band[7] at 1360 and 1364 cm.$^{-1}$,

* Part XXI, preceding Paper.

[1] Satoh, Ishii, Oyama, and Okumura, *J. Pharm. Soc. Japan*, 1955, **75**, 1573; Satoh, Ishii, Oyama, Wada, and Okumura, *Chem. and Pharm. Bull. (Japan)*, 1956, **4**, 284; 1957, **5**, 253.

[2] Tschesche, Lipp, and Grimmer, *Annalen*, 1957, **606**, 160; Tschesche and Lipp, *ibid.*, 1958, **615**, 210.

[3] Satoh, *Chem. and Pharm. Bull. (Japan)*, 1960, **8**, 270.

[4] Satoh, *Chem. and Pharm. Bull. (Japan)*, 1962, **10**, 43.

[5] Tschesche, Hammerschmidt, and Snatzke, *Annalen*, 1961, **642**, 199.

[6] Shoppee and Lack, preceding Paper.

[7] Jones, R. N., and Cole, *J. Amer. Chem. Soc.*, 1952, **74**, 5648.

respectively, in the infrared spectra of **14α-** and **14β-digiprogenin**, is supported by the n.m.r. spectrum of **14α-digiprogenin** (I; R = H). The signal for the 20-methyl group appears as a sharp singlet for three protons at τ 7·66; this is in excellent agreement with the usual value (7·7) for **17α-hydroxypregnan-20-ones**, and occurs at the same position (7·68) as in the spectra of **14α-digacetigenin** (IV; R^1 = H, R^2 = Ac) and its 3-acetate.[6]

The optical rotatory dispersion curve for **14α-digiprogenin** (I; R = H) closely resembles those for **14α-digacetigenin**[6] (IV; R^1 = H, R^2 = Ac) and deacetyl-**14α-digacetigenin**[6] (IV; R^1 = R^2 = H), and suggests that these compounds are 17β-hydroxy-17α-pregnan-20-ones. The small molecular amplitude observed ($10^{-2}a$ -39) is in better agreement with the calculated value[8] for an 11,15,20-trioxo-14α,17α-structure ($10^{-2}a$ $+24$) * than with an 11,15,20-trioxo-14α,17β-structure (calc. $10^{-2}a$ $+297$).*

The foregoing evidence indicates that **14α-digiprogenin** is 3β,17β-dihydroxy-14α,17α-pregn-5-ene-11,15,20-trione (I; R = H).

EXPERIMENTAL

The nuclear magnetic resonance spectrum was determined on a Varian D.P. 60 instrument at 60 Mc./sec with deuteriochloroform as solvent and tetramethylsilane as internal reference; the optical rotatory dispersion curve was measured using a Rudolph polarimeter.

("γ")-14α-*Digiprogenin* (I; R = H).—The n.m.r. spectrum showed three signals, each corresponding to three protons and assigned as follows: 13-methyl at τ 8·91, 10-methyl at 8·89, and 20-methyl at 7·66. The spectrum was also determined in pyridine, and signals were observed for the 13-methyl at 8·78, the 10-methyl at 8·72, and the 20-methyl at 7·72. Optical rotatory dispersion in MeOH: [M] -1700 (336 mμ, trough), $+2200$ (305 mμ, shortest wavelength measured); $10^{-2}a$ -39. The 3-acetate gave signals at τ 8·89 (13-Me), 8·89 (10-Me), 7·96 (3-COMe), and 7·66 (20-Me).

("α")-14β-*Digiprogenin* (II; R = H).—This was even more insoluble than the 14α-epimer. The n.m.r. spectrum showed two signals, each corresponding to 3 protons, at τ 8·83 (10-Me) and 8·65 (13-Me). The 3-acetate gave signals at τ 8·83 (10-Me), 8·66 (13-Me), 7·96 (3-COMe), and 7·73 (20-Me).

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* The standard value for the rotatory dispersion contribution of an 11-carbonyl group in saturated 5α,14α- and 5β,14α-steroids is $10^{-2}a$ $+12$ but in Δ⁵-14α-steroids rises to $10^{-2}a$ $+50$.[9]

[8] Djerassi, "Optical Rotatory Dispersion," McGraw-Hill, London, 1960, pp. 71, 72.
[9] Shoppee and Lack, *J.*, 1962, 3624.