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Structure of Purprogenin

In 1960, Satoh, *et al.*, reported the isolation of purpronin from *Digitalis purpurea* L.,1) which upon acid hydrolysis, afforded purprogenin (1) that was correlated to purpnigenin.1) The structure of purpnigenin was established as 3β,14β,15α-trihydroxypregn-5-en-20-one by synthetic way.2) The position of the additional carbonyl group was assigned to be at C-12 due to the stability on alumina.3)

We now wish to describe the establishment of the position of the carbonyl group by partial synthesis of 14β,15α-dihydroxy-5-pregna-3,12,20-trione (Ⅷ) from hecogenin acetate. Hecogenin acetate was converted to 3β,12β-dihydroxy-5α-pregn-16-en-20-one-3-monoacetate (Ⅱ) according to the procedures by Cameron, *et al.*,4) and Adams, *et al.*,5) and this product was treated with dibromodimethylhydantoin to give 3β,12β-dihydroxy-5α-pregn-14,16-dien-20-one-3-monoacetate (Ⅲ),*1 m.p. 223~225°, $[\alpha]_D^{20}$ +288° (c=0.28 in $CHCl_3$), $C_{23}H_{32}O_4$, UV λ_{max}^{EtOH} mμ (log ε): 315 (4.01), IR ν_{max}^{Nujol} cm^{-1}: 3460 and 3340 (OH), 1736 (OAc), 1610 and 1518 (conjugated dienone system), NMR ($CDCl_3$) τ: 9.02 (19-CH_3), 8.88 (18-CH_3), 7.55 (21-CH_3), 6.95 (1H, q, J=11 c.p.s., 8 c.p.s., 12α proton), 3.89 (1H, t, J=2 c.p.s., 15-vinyl proton), 2.57 (1H, d, J=2 c.p.s., 16-vinyl proton). Epoxidation of Ⅲ with monoperphthalic acid gave the 14β,15β-epoxide (Ⅳ), m.p. 180~182°, $[\alpha]_{589}$ +52.6° (c=0.19 in dioxane), $C_{23}H_{32}O_5$, UV λ_{max}^{EtOH} mμ (log ε): 242 (3.93), IR ν_{max}^{Nujol} cm^{-1}: 3460 (OH), 1735 (OAc), 1655 and 1585 (α,β-unsaturated ketone system), NMR ($CDCl_3$) τ: 9.08 (19-CH_3), 8.74 (18-CH_3), 7.58 (21-CH_3), 6.1 (1H, d, J=1.5 c.p.s., 15-proton bearing epoxide), 2.82 (1H, d, J=1.5 c.p.s., 16-vinyl proton), ORD6): (c=0.19 in dioxane), $[\alpha]_{313}$ (peak) +652.6°, $[\alpha]_{362}$ (trough) −355.2°. The configuration of the epoxide was considered to be 14β,15β-type since the compound (Ⅳ) could be converted to 3β,12β,14β-trihydroxy-5α-17-isopregnan-20-one-which had a stable configuration7) of the 17-side chain with a C/D *cis* juncture. The cleavage of the epoxide ring in Ⅳ with sulfuric acid in dioxane gave Δ^{16}-triol (V), m.p. 273~275°, $[\alpha]_{589}$ +75° (c=0.1 in dioxane), $C_{23}H_{34}O_6$, UV λ_{max}^{EtOH} mμ (log ε): 234.5 (3.83), IR ν_{max}^{Nujol} cm^{-1}: 3500 and 3300 (OH), 1745 (OAc), 1645 and 1610 (α,β-unsaturated ketone system), NMR ($CDCl_3$) τ: 9.15 (19-CH_3), 8.88 (18-CH_3), 7.52 (21-CH_3), 5.32 (1H, d, J=3 c.p.s., 15β proton), 3.3 (1H, d, J=3 c.p.s., 16 proton), ORD6): (c=0.1 in dioxane), $[\alpha]_{300}$ (peak) +2750°, $[\alpha]_{350}$ (trough) −1600°. These data indicate that the cleavage of the 14β,15β-epoxide of Ⅳ afforded a 14β,15α-*trans*-diol grouping, as we reported.8)

By hydrogenation with 5% palladium-charcoal in ethyl acetate-ethanol (1:1), V afforded the saturated triol (Ⅵ), which had a negative Cotton effect in ORD curve. Treatment of Ⅵ with 5% methanol-KOH afforded Ⅶa and Ⅶb (4:6). Ⅶa: m.p. 236~238°, $C_{21}H_{34}O_5$, IR ν_{max}^{Nujol} cm^{-1}: 3500, 3380 and 3300 (OH), 1700 (side chain ketone), ORD: (c=0.1 in MeOH),

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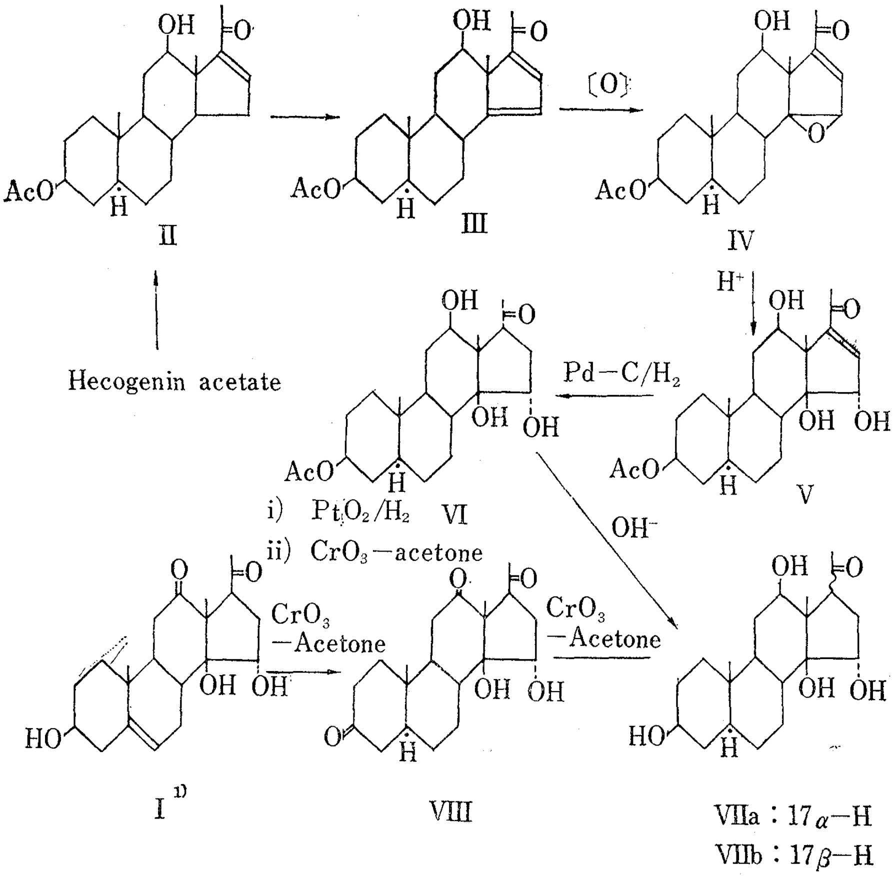
*1 Satisfactory analytical results wers obtained for all compounds described in this communication. All melting points were measured with a Kofler Hot Stage Microscope and are uncorrected.

1) D. Satoh, H. Ishi, Y. Oyama: This Bulletin, **8**, 657 (1960).
2) H. Ishi: *Ibid.*, **9**, 411 (1961).
3) D. Satoh: Ann. Report of SHIONOGI Research Laboratory, **14**, 36 (1964).
4) A.F.B. Cameron, R.M. Evans, J.C. Hamlet, J.S. Hunt, P.G. Tomes, A.G. Long: J. Chem. Soc., **1955**, 2807.
5) W.J. Adams, D.N. Nirk, D.K. Patel, V. Petrow, I.A. Stuart-Webb: *Ibid.*, **1955**, 870.
6) The ORD curve of the 12β-acetoxy or 12-nonsubstituted 14β,15β-epoxy-5α-pregn-16-en-20-one showed a positive Cotton effect and ORD curve of the 12β-acetoxy or 12-nonsubstituted-14β,15α-dihydroxy-5α-pregn-16-en-20-one showed a negative Cottone effect, unpublished data. The negative Cotton effect of the compound (Ⅳ) would be due to the action of the 12β hydroxyl group.
7) H. Mitsuhashi, T. Nomura, M. Fukuoka: Steroids, **4**, 483 (1964).
8) H. Mitsuhashi, M. Fukuoka: This Bulletin, **14**, 809 (1966).

$[\alpha]_{265}$ (trough) −900°, $[\alpha]_{305}$ (peak) +1500°, $[\alpha]_{589}$ +100°. VIIb: m.p. 219~222°, $C_{21}H_{34}O_5$, IR ν_{max}^{Nujol} cm^{-1}: 3400 (broad) (OH), 1685 (side chain ketone), ORD: (c=0.067 in MeOH), $[\alpha]_{256}$ (peak) +2037.5°, $[\alpha]_{300}$ (trough) −1052.2°, $[\alpha]_{589}$ +44.7°.

Oxidation of VIIa with chromium trioxide in acetone[9] gave a trione (VIII), m.p. 238.5~240.5°, $C_{21}H_{30}O_5$, IR ν_{max}^{KBr} cm^{-1}: 3440 (OH), 1700 (6-membered ring ketone and side chain ketone), NMR ($CDCl_3$) τ: 8.90 (19-CH_3), 8.84 (18-CH_3), 7.63 (21-CH_3), 5.72 (1H, q, J=6.7, 2 c.p.s., 15β proton), ORD: (c=0.081 in MeOH), $[\alpha]_{263}$ (trough) −3506.1°, $[\alpha]_{305}$ (peak) +3703.7°, $[\alpha]_{589}$ +148.1°. These characteristics correspond to the formula VIII.



On the other hand purprogenin was hydrogenated with Adams catalyst in acetic acid, and subsequently oxidized with chromium trioxide in acetone[9] giving a trione (VIII), which was proved to be identical with the trione (VIII) derived from hecogenin by mixed melting point, comparisons of thin-layer chromatography, mass spectra, and IR spectra. This result established the position of the additional carbonyl group in purprogenin being at C-12.

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[9] A solution of 5.3 g. CrO_3 and 8.0 g. H_2SO_4 in 40 ml. H_2O.