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Studies on Digitalis Glycosides. The Structure of Purprogenin

Previously, our group[1-4] proposed the structure 3β,14,15α-trihydroxy-14β, 17β-pregn-5-ene-12,20-dione (I) for purprogenin, a C_{21}-steroid of *Digitalis purpurea* L. leaves, but there remains the establishment of the location of a six-membered ring ketone and the configuration of C-17 side chain by stronger evidence. Recent works on the structure proof of purprogenin by the correlation of the genin and hecogenin[5] as well as digacetigenin[6,7] prompted us to report our own interconversion of purprogenin and digipurpurogenin-II[8] (isoramanone,[8] V).

Purprogenin (I) was hydrogenated with platinum catalyst in acetic acid to saturate 5,6-double bond, giving, after oxidation with Kiliani's reagent, a hydroxy-tetraketone (IV), mp 262—265°, $C_{21}H_{28}O_5$, $[\alpha]_D^{24}$ +101.3±6.1°(c=0.232, $CHCl_3$); NMR ($CDCl_3$) τ: 8.95 (19-CH_3), 8.73 (18-CH_3), 7.62 (21-CH_3); IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3293 (14β-OH), 1747 (15-ketone), 1707, 1698 (20-ketone). Since the IR band at 1707 cm^{-1} has twice intensity of absorption at 1698 cm^{-1}, it is ascribable to 3-ketone and the six-membered ring ketone in question, which is probably located at C-12. A/B-ring juncture was shown by CD determination: the difference between the molecular elipticity of IV ([θ] +12417 (291 mμ)) and that of its 3-hemiketal[9,10] ([θ] +9313 (290 mμ)) is Δ[θ] +3104 and this positive contribution due to 3-ketone indicates that A/B-ring juncture is *trans*. This hydroxy-tetraketone was the substance which we wish to derive from digipurpurogenin-II (V) of known structure.

Digipurpurogenin-II diacetate (Vb) was submitted to catalytic hydrogenation with platinum in acetic acid and the crude product was oxidized with Kiliani's reagnet to give a dihydro derivative (VI), mp 165—167°, $C_{25}H_{38}O_6$. The signal of 3α-proton in NMR

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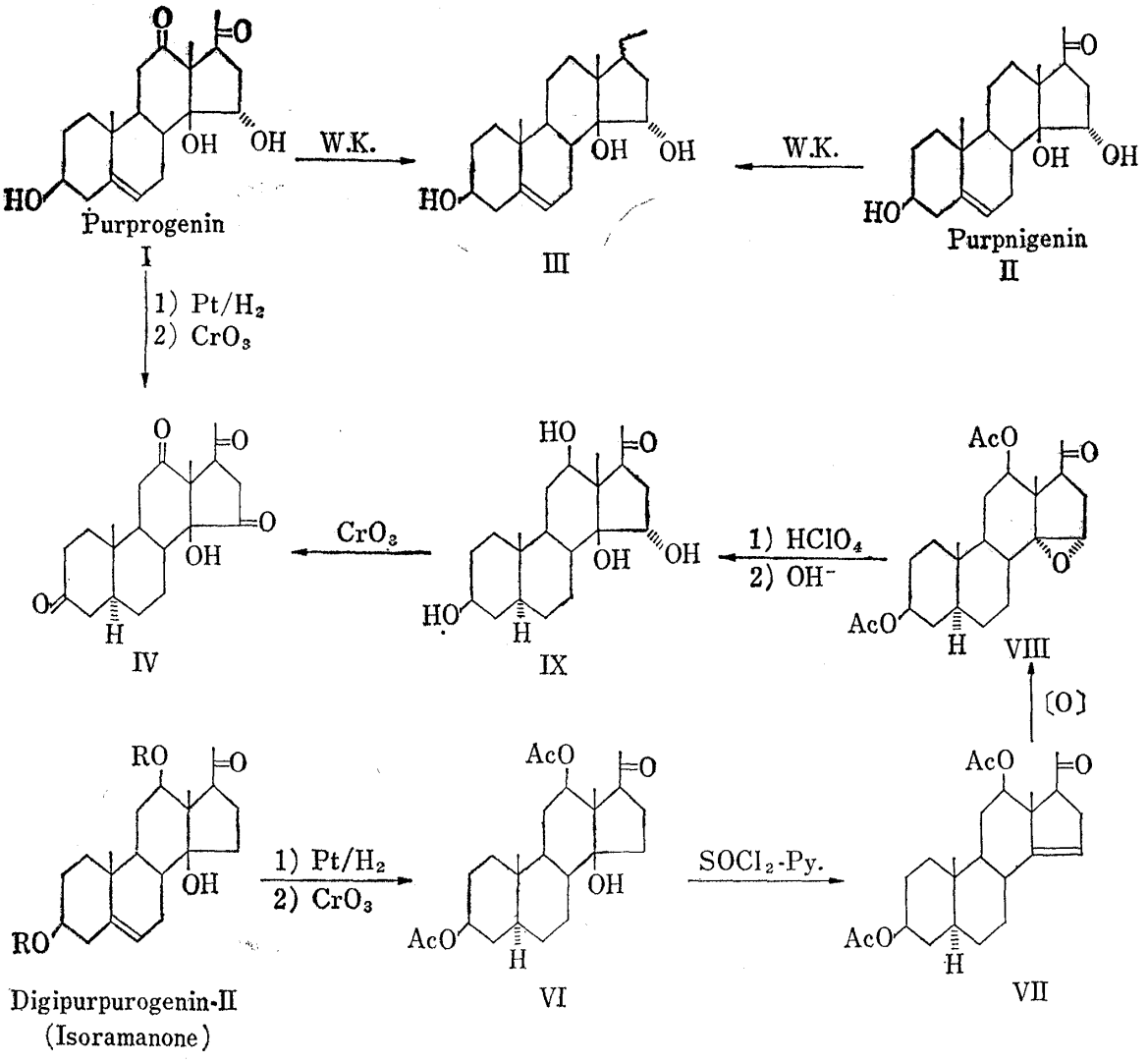

Va : R=H, Vb : R=Ac

spectrum appears as a broad multiplet, showing that the A/B-ring juncture of VI is *trans*. Dehydration of VI with thionyl chloride in pyridine afforded an amorphous 14-anhydro derivative (VII), UV λ_{max}^{EtOH} mμ (ε): 201 (6900), which was oxidized with *m*-chloroperbenzoic acid to give a 14,15-epoxide (VIII), mp 137—140°, $C_{25}H_{36}O_6$, $[\alpha]_D^{24}$ +34.1±3.3° (c=0.226, $CHCl_3$); NMR ($CDCl_3$) τ: 9.14 (18-CH_3), 9.08 (19-CH_3), 8.01, 7.98 (2Ac), 7.91 (21-CH_3), 6.60 (15β-H). Since oxidation of 14,15-unsaturated steroids having 17β-side chain with peracid has been known to afford 14α,15α-epoxy derivatives,[11-15] the compound VIII must be 14α,15α-epoxide. The above NMR data support this assignment. Cleavage of the epoxide ring in VIII with 0.7% perchloric acid in acetone at room temperature for four days[16] and subsequent deacetylation with 0.15% potassium hydroxide in methanol at the same temperature for two hours[16] afforded a crude tetrahydroxy-ketone (IX) as a main product, $[\alpha]_D^{23}$ +94.2±4.5°(c=0.257, MeOH). The 20-ketone in IX gave positive Cotton effect in

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CD, $[\theta]$ +676 (285 mμ), showing the 17–side chain to be β–oriented. As the cleavage of 14α,15α–epoxide with acid generally gives rise to 14β,15α–glycol,[11-15] the structure IX was assigned to the tetrahydroxy–ketone.

Oxidation of IX with Kiliani's reagnet gave a hydroxytetraketone, mp 262—266°, $C_{21}H_{28}O_5$, $[\alpha]_D^{23}$ +104.3±6.1° (c=0.235, $CHCl_3$). The IR spectrum in chloroform shows absorptions at 3281 (14β–OH), 1747 (15–ketone), 1707 (3– and 12–ketone) and 1697 cm^{-1} (20–ketone). Inspection of the IR spectrum in detail showed the presence of a strong hydrogen bonding between 14β–hydroxyl group (3281 cm^{-1}) and 20–carbonyl group (1697 cm^{-1}), giving further evidence that 17–side chain has the β–configuration. This product having 12–ketone and 17β–methyl ketone grouping proved to be identical with the hydroxy–tetraketone (IV) derived from purprogenin by mixed melting point and comparisons of TLC and IR spectra. These results established the structure of purprogenin to be 3β,14,15α–trihydroxy–14β,17β–pregn–5–ene–12,20–dione (I) as previously proposed by our group.

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A Novel Rearrangement of a Quinol Acetate[1]

Quinol acetates[2] prepared by the reaction of phenols with $Pb(OAc)_4$ are known to be rearranged to hydroquinones[3] under conditions of the Thiele reaction (Ac_2O–concd. H_2SO_4). We attempted to apply this method to tetrahydroisoquinolines in order to introduce hydroxyl group to benzene ring and chose corypalline (I) as a starting material.

Unexpectedly, we encountered a novel rearrangement, in which acetoxyl group moved to 4–position instead of 5–position (normal rearrangement).

A solution of I (200 mg, *ca.* 1 mmole) and $Pb(OAc)_4$ (680 mg, *ca.* 1.5 mmole) was stirred for 1.5 hour at room temperature, treated with ice–water, basified with $NaHCO_3$, and extracted with $CHCl_3$. Chromatography of the $CHCl_3$ layer on neutral Al_2O_3 (Woelm, elution with $CHCl_3$) gave N–methyl–10–acetoxy–6–methoxy–7–oxo–$\Delta^{5,6,8,9}$–hexahydroisoquinoline (II), mp 118—120° from *n*–hexane, (72 mg, 20%) [*Anal.* Calcd. for $C_{13}H_{17}O_4N$: C, 62.14; H, 6.82; N, 5.57. Found: C, 62.34; H, 6.94; N, 5.63. NMR τ: 7.92 (S., OAc), 7.61 (S., =NMe), 7.06, 6.68 (each d., C–1 *gem.* protons, J=12 cps), 6.34 (S., OMe), 4.20 (S., a vinylic proton), 3.82 (d., a vinylic proton, J=1.5 cps). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1745 (OAc), 1675, 1655, 1630 (dienone)].

A mixture of quinol acetate (II)(275 mg, *ca.* 1.1 mmole) in Ac_2O (4 ml) and concd. H_2SO_4 (0.3 ml) in Ac_2O (1 ml) was stood for 2 hours at room temperature. After adding crushed ice to the reaction mixture and extracting excess Ac_2O with ether, H_2O layer was

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