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ON THE UNEXPECTED IDENTITY OF THEASAPOGENOL D (=CAMELLIAGENIN A), A MINOR SAPOGENOL OF TEA SEEDS, WITH DIHYDROPRIVEROGENIN A.

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In the previous papers, we assigned the structures of theasapogenols A, B (=barringtogenol C), E as I[1], II[2], III[3], and also reported[2,3] the isolation of two minor theasapogenols designated as C and D from the seeds of Thea sinensis L. Later on, theasapogenols C and D have been identified by their direct comparisons* (mixed mp., IR and TLC) respectively with camelliagenins C and A**, whose structures have been proposed as IV and V having 22α-OH (equatorial) functionality by two Japanese groups[4]. On the other hand, in connection with the studies on saponins obtainable from some Japanese Primulaceous plants, we have isolated[5] primulagenin A and dihydropriverogenin A, which was initially isolated by Tschesche and co-workers from European Primulaceous plants and assigned as VI possessing 22β-OH (axial) function[6]. On comparison of theasapogenol D with dihydropriverogenin A, we unexpectedly found that the both compounds are identical (mixed mp., IR, and TLC). Therefore, we wish to describe in the present communication our remarks on the configuration of 22-OH functionality of theasapogenol D verifying additionally α (equatorial) to be correct and consequently wish to revise the structures of priverogenins A and B (initially proposed as VII and VIII by Tschesche et al.[6]) to IX and X.

On treatment with acetone and anhydrous $CuSO_4$, theasapogenol D (V) afforded two monoacetonides: viz. 16,22-di0- and 22,28-di0- isopropylidene derivatives (XI and XII), analogously as in the cases of theasapogenols A (I) and B (II), which carry 16α,22α,28-triol functions***. As the configuration

* Although the name camelliagenins (or dihydropriverogenin A instead of camelliagenin A) should be preferred for these compounds, we use the name theasapogenols only in this paper, so that we could postulate our findings without complexity.

** In the recent communication, Ito et al. also reported[7] the isolation of camelliagenin A from the seeds of Thea sinensis L.

*** The previous workers[4] prepared only XI from camelliagenin A (=theasapogenol D), however we isolated XI and XII similarly as in the cases of theasapogenols A and B. The structures were characterized by NMR spectra of acetyl derivatives of XI and XII, which will be reported in our full paper.

at C_{22} of theasapogenol B (II) has been proved rigidly[2,8], the unambiguous conversion of II into theasapogenol D (V) was performed by the reaction sequences as shown below.

Thus, 3-O-acetyl-28-O-trityl-16,22-diO-monoacetonide (XIII), which was prepared from II by successive treatment with trityl chloride-pyridine, acetone-anhydrous $CuSO_4$, and by mild acetylation, furnished a ketone (XIV); IR (CCl_4): 1730, 1720, 1243 cm^{-1}, on CrO_3-pyridine oxidation. The latter was then subjected to deacetonidation under a mild acidic condition giving XV. Finally the Huang-Minlon reduction of XV followed by detritylation afforded as a major product 21-desoxy-theasapogenol B, which was proved to be identical with theasapogenol D (V) in all respects. The carbonyl function at C_{21} of XIV resisted strikingly to the Huang-Minlon reduction probably due to the sterical congestion. As 22-OH must retain in the stable equatorial orientation during the procedure from XIV to V, the conversion described here coupled with the behavior of theasapogenol D on acetonide formation provides the additional support for 22α-OH (equatorial) in V*.

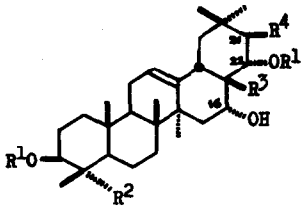
As mentioned before, Tschesche and co-workers proposed[6] the structures of dihydropriverogenin A as VI having 22β (axial)-OH function. Their conclusion was mostly based on the fact that $NaBH_4$ reduction of 22-keto derivative (XVI) yielded 22-epimer as the major product. They assumed that the major product must have α-equatorial configuration (XVIII), so that the original alcohol should be β-axial at C_{22} (as XVII, VI). We reinvestigated on this point as described below.

By passing through the neutral alumina (Woelm) column in benzene solution, theasapogenol D triacetate (XIX) suffered both acyl migration and deacetylation yielding 3,16,28-triO-acetate (XX) and 3,16-diO-acetate (XXI) in good yield**. The former was next oxidized by CrO_3 to give 22-keto-triacetate (XVI), which on reduction with $NaBH_4$ followed by an alkaline treatment furnished 22-epi-theasapogenol D (major) (XXII) and V (minor) as reported by Tschesche and co-workers[6]. The acetylation of the epimer with acetic anhydride and pyridine at room temperature gave a triacetate (XXIII), whose NMR spectrum together with the spectrum of XIX are as shown in Table I.

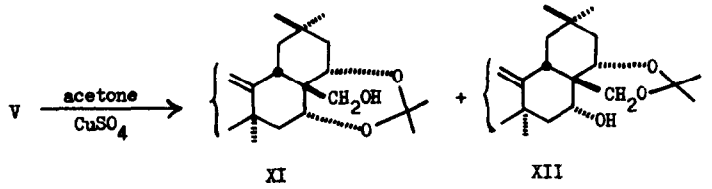
The multiplet signal assignable to 22-H of XXIII appeared with a half band width less than 10 cps. suggesting 22-H to be in an equatorial configuration, while the signal due to 22-H of XIX was obtained as a quartet supporting the aforementioned assignment. Furthermore, the findings that the line position of 16-H in XXIII existed at 15 cps. higher field than that of XIX (perhaps due to lack of shielding effect existed in XIX caused by C_{22}-equatorial oxygen function) and the non-equivalency

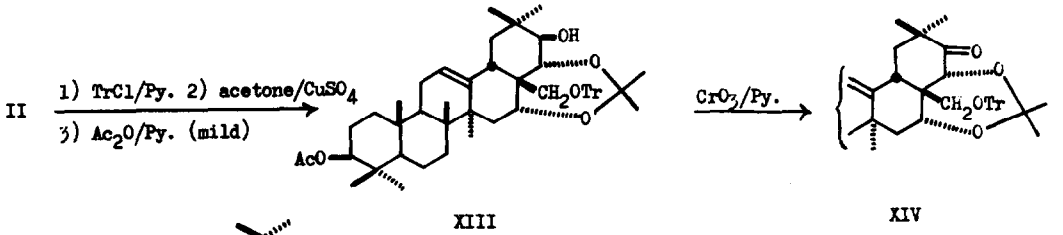
* The facile acyl migration of XIX (from 22-O to 16-O) described later is also illustrative of 22α-OH in V.

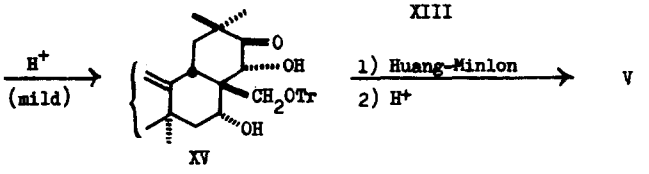
** The structural determination of these acetates was performed by their NMR spectral analyses. The similar acyl migrations of other theasapogenols are now under study in this laboratory.

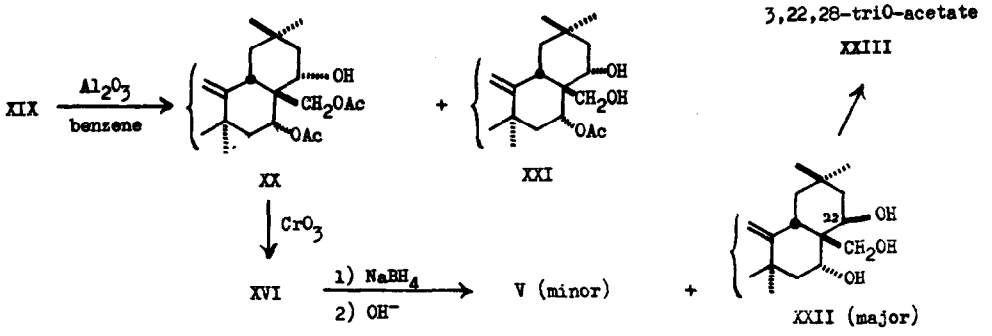


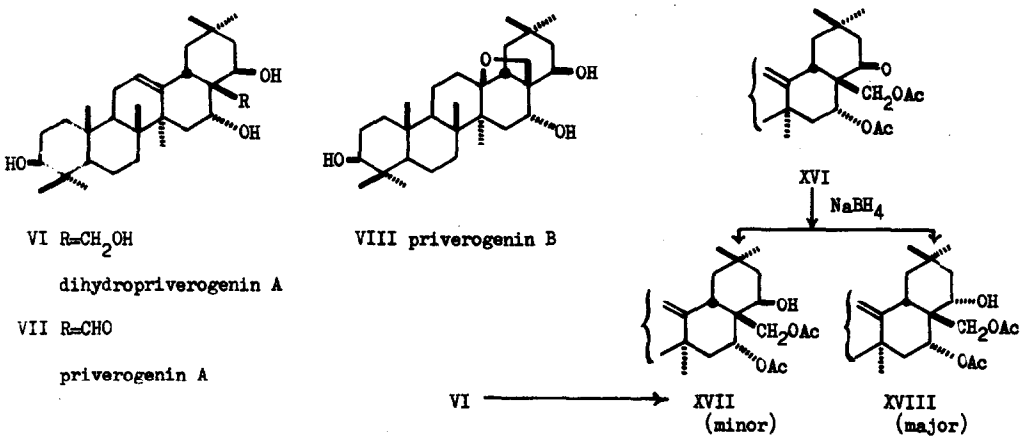
	R^1	R^2	R^3	R^4	
I	H	CH_2OH	CH_2OH	OH	theasapogenol A
II	H	CH_3	CH_2OH	OH	theasapogenol B (=barringtogenol C)
III	H	CHO	CH_2OH	OH	theasapogenol E
IV	H	CH_2OH	CH_2OH	H	theasapogenol C (=camelliagenin C)
V	H	CH_3	CH_2OH	H	theasapogenol D (=camelliagenin A, dihydropriverogenin A)
IX	H	CH_3	CHO	H	priverogenin A
X	H	CH_3	13β,28-oxido- (without Δ^{12})	H	priverogenin B
XIX	Ac	CH_3	CH_2OAc	H.	











Structures proposed by the previous workers[6]

Table I. (τ values in $CDCl_3$ at 100 Mc.)

	XIX	XXIII
$>C_{(3)}\underline{H}OAc$	5.50 (t.-like)	5.50 (t.-like)
$>C_{(16)}\underline{H}OH$	5.76 (m.)	5.91 (m.)
$>C_{(22)}\underline{H}OAc$	4.69* (q., J=6 and 12 cps.)	4.67** (t.-like, $W\frac{h}{2}<10$ cps.)
$-C_{(28)}\underline{H_2}OAc$	H_A=6.34, H_B=6.23 (ABq., J=11 cps.)	H_A=6.20, H_B=5.99 (ABq., J=12 cps.)
$=\overset{|}{C}_{(12)}\underline{H}$	4.68 (m.)	4.67 (m.)

* Although the signal was overlapped by that of C_{12}-proton, the quartet was clearly distinguished.

** The actual $W\frac{h}{2}$ value of this signal seems to be as small as for the ordinary equatorial proton[9], however the multiplet due to C_{12}-proton appearing at the similar chemical shift again disturbed to read such a reasonable value.

of methylene protons attached to C_{28} increased in XXIII comparing to XIX (due to voluminous C_{22}-axial function nearby; the chemical shift differences between H_A and H_B are 0.21 ppm. in XXIII, 0.11 ppm. in XIX), could rationally be explained by assigning equatorial 22-OAc in XIX and axial one in XXIII. It follows that $NaBH_4$ reduction of the ketone (XVI) afforded the axial alcohol (XXII) as the major product contrary to the previous assumption[6] and the configuration of 22-OH in theasapogenol D (=dihydropriverogenin A) must be α-equatorial.

Accordingly, the structures VII and VIII originally proposed to priverogenins A and B by the previous workers[6] should be replaced by IX and X.

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