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THEASAPOGENOL B*(= BARRINGTOGENOL C), THE SECOND MAJOR TRITERPENIC ALCOHOL FROM THE SEEDS SAPONIN OF THEA SINENSIS L.

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In 1954, Y. Ueda reported[1] the isolation and some chemical studies on thea-sapogenol, a triterpenic sapogenin originated from the seeds saponin of Thea sinensis L. (Japanese name "Cha"). However, no work thereafter has been presented on the structural study of the sapogenol. With the generous agreement of Dr. Ueda, the chemical and some biological studies on thea-saponin have been performed in this laboratory. It has been found that the sapogenol** consists mainly of four components designated theasapogenol A (major), B(second major), C, and D according to their Rf values from the bottom on TLC. The present and following communications deal with the chemical studies on theasapogenol B (I) and theasapogenol A respectively.

Theasapogenol B (I), $C_{30}H_{50}O_5$***, mp. 278-284°; $[\alpha]_D$ +11°(c, 0.5;pyridine);

* Although the identity between theasapogenol B and barringtogenol C was established as discussed in the later part of the paper, we use the name theasapogenol B for the discussion here.

** The sapogenol mixture was obtained by acid hydrolysis of the saponin followed by alkaline treatment.

*** All the compounds described with chemical formulae gave satisfactory analytical data. Melting points were taken on the Yanagimoto micromelting point apparatus (a hotstage type) and recorded uncorrected. Specific rotations were taken in $CHCl_3$(c, 0.5), IR and NMR spectra were measured in KBr and $CDCl_3$(60 Mc) unless specified otherwise.

IR: 3367, 1634 cm^{-1}, gave a triacetate (II), $C_{36}H_{56}O_8$, mp. 244-6°; $[\alpha]_D$ +15°, and a tetraacetate (III), $C_{38}H_{58}O_9$ (M^+ 658), mp. 222-224°; $[\alpha]_D$ +20°, on mild acetylation. On the other hand, under more forcing condition, it afforded a pentaacetate, exhibiting no hydroxylic absorption band in the IR spectrum. Chromium trioxide oxidation of III in pyridine yielded a monoketone (IV), $C_{38}H_{56}O_9$, mp. 276-277°; $[\alpha]_D$ -34°; IR: 1739, 1718(sh.) cm^{-1} (acetyl and six-membered ring carbonyls respectively), no OH. It would reasonably be assumed, that the sapogenol B possesses one hindered, probably axial, secondary hydroxyl group. The NMR spectrum (Table 1) of III shows the existence of one primary and three secondary acetoxyl groups, among which two are situated in a vicinal position with trans diequatorial configuration estimated from its coupling constant (τ_A: 4.40, τ_B: 4.54 in AB quartet, J=10 cps.) due to the hydrogens attached to the carbons bearing acetoxyl groups. Furthermore, two doublets centered at τ 6.06 (1H) and τ 4.73 (1H) with J=10 cps. in the NMR spectrum of II reveals that one of α-glycolic hydroxyls is not acetylated. On treatment with alkaline, IV liberated CH_2O, thus indicating I has a partial structure (V).

Treatment of I with acetone and p-TsOH (catalytic amount) furnished two monoacetonides, suggesting three or four hydroxyls are located in a proximity

Table 1. NMR signals of III and VII (τ-values).

	III	VII	
>CH-OAc(eq.)	5.45 (t.-like)	5.48 (t.-like)	
>CH-OH (ax.)	5.77 (m.)	5.15 (m.)*	
a vinyl proton	4.60 (m.)	4.68 (m.)	
—C-CH$_2$-OAc	6.30 (s.)	—C-CH$_2$-O-C(CH$_3$)$_2$	6.50 (s.)
HC-OAc	4.54 (AB q. J=10 cps.)	HC—O	6.14 (d., J=10 cps.)
HC-OAc	4.40	HC—OAc	4.38 (d., J=10 cps.)
—C—		—C—	

* Deshielded probably by a neighbouring oxygen function of the acetonide linkage.

to form the acetonide linkages. Acetylation of the major product (VI) gave a monoacetonide-diacetate (VII), whose NMR spectrum indicates that the isopropylidene linkage is formed between one of the α-glycolic hydroxyls and the primary hydroxyl function based on the signals at τ 6.14 (1H, d., J=10 cps.) ascribed to a methine proton of the glycol and at τ 6.50 (2H, s.) assignable to the methylene protons of the primary alcohol, which was shielded by 0.2 ppm. compared to the signal in III (Table 1.). Therefore, both hydroxyls joined to the acetonide formation could be in a 1,3-position, thus extending their partial environment to VIII.

The mass spectrum of IV demonstrates the retro Diels-Alder fragments at m/e 406 (a) and 249 (b), characteristic to a α-or β-amyrin skeleton[2], together with a molecular ion at m/e 656. It follows that ring A or B in IV possesses only one acetoxyl function whereas the remaining functions locate in rings D and E. The β-amyrin skeleton can be preferred for theasapogenol B deduced by the C-methyl signal patterns (seven methyls without coupling) in the NMR spectra of all its derivatives. When a proton signal appearing at τ 5.45[3] (1H, t.-like, $w_{\frac{1}{2}}$=17 cps.) of III is attributed to 3α-H based primarily on a biogenetical viewpoint, theasapogenol B could now be expressed by either I or I'.

The dehydration of II with $POCl_3$-pyridine resulted an anhydro-triacetate (IXa), $C_{36}H_{54}O_7$, mp. 221.5-223°; $[\alpha]_D$ +65°, exhibiting NMR signals at τ 5.71 (1H at C_{16}, m.), and τ 4.71 (1H at C_{22}, s.) (Table 2.), which suggested a system (XII) in IXa. The Kiliani oxidation of IXb with a subsequent methylation

Table 2. NMR signals of IXa (τ-values).

>C<u>H</u>-OAc(eq.)	5.47 (t.-like)	C-<u>H</u>	6.39 (s.)
a vinyl proton	4.71 (m.)	<u>H</u>-C-OAc	4.71 (s.)*
		C-C<u>H</u>$_2$-OAc	6.06 (AB q., J=12 cps.)
		C-<u>H</u>	5.71 (m.)

* Since this is a prominent signal, it is easily discriminated from the multiplet due to a vinyl proton.

afforded a diketo-methylester* (XI); IR (CCl_4): 1773, 1743, 1710 cm^{-1}(attributable to five membered ring, methyl ester, and six membered ring carbonyls respectively), which supports an assumption of IX having a five membered ether linkage. Although for the possible structure of the anhydro-triacetate, IX'a could not be ruled out at this stage of discussion, an inspection with a Dreiding model on the dihedral angle between C_{15} and C_{16} protons of IX'a discloses the NMR signal due to C_{15}-H would not appear as a singlet. In IXa, however, the dihedral angle** between C_{21}-H and $C_{22}\beta$-H is found nearly 90°, corroborating both hydrogens appeared as two singlets (τ 6.39 and τ 4.71). The structure of theasapogenol B could consequently be presented as I***.

Checking the literature it has been found that the anhydro derivative (IXa) is epimeric at C_{22} with barringtogenol D triacetate, whose structure has been proposed as Xa by Chakraborti and Barua[4]. On comparison of the physical properties of IXa with barringtogenol D triacetate (Xa), which was kindly supplied by Dr. Barua, we found both samples identical (mixed mp., IR, and TLC).

The observations led us to expect the identity of theasapogenol B with barringtogenol C (=aescinidin), and the comparison (mixed mp., IR, and TLC) of the corresponding tetraacetates (III and aescinidin tetraacetate****) surprisingly proved the correctness of the above assumption. Therefore, the structure (I) proposed for theasapogenol B in this paper seems to represent the structure of barringtogenol C (=aescinidin) rather than the already proposed structure having the trans diaxial hydroxylic functions ($C_{21}\alpha$-OH, $C_{22}\beta$-OH in I)[5].

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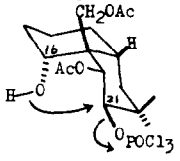
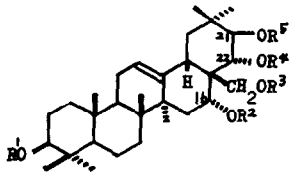
* In ref. 4), the IR absorption bands for the corresponding compound were 1765, 1725, 1700 cm^{-1}(the state was not specified).

** The dihedral angle between C_{21}-H and $C_{22}\alpha$-H (as in Xa) is close to 30°, which is expected to give J value of 7 cps(M.Karplus, J.Am.Chem.Soc., 85 2820(1963)).

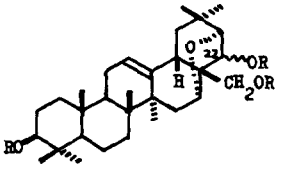
*** The mechanism for the formation of the anhydro derivative (II→IXa) could be accounted by an intramolecular SN_2 type process.



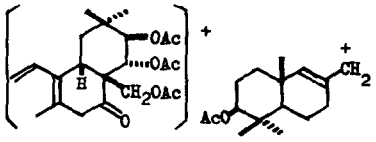
**** Aescinidin used here for comparison was obtained in this laboratory from the hydrolysed mixture of the seeds saponin of Japanese Aesculus turbinata BLUME along with protoaescigenin and aescigenin (6).



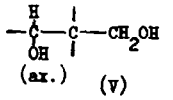
(I) R¹, R², R³, R⁴, R⁵ = H
theasapogenol B
(II) R¹, R³, R⁴ = Ac, R², R⁵ = H
(III) R¹, R³, R⁴, R⁵ = Ac, R² = H
(IV) R¹, R³, R⁴, R⁵ = Ac, CO at C-16
(VI) R¹, R², R⁵ = H, R³, R⁴ = 
(VII) R¹, R⁵ = Ac, R² = H, R³, R⁴ = 



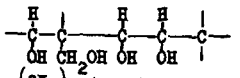
(IX) a: R = Ac, C_{22}α-OAc
b: R = H, C_{22}α-OH
(anhydro-theasapogenol B)
(X) a: R = Ac, C_{22}β-OAc
b: R = H, C_{22}β-OH
(barringtogenol D)



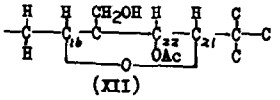
a) m/e 406 b) m/e 249



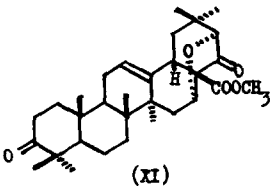
(ax.) (V)



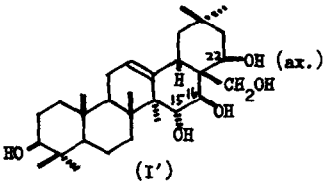
(ax.) (VIII)



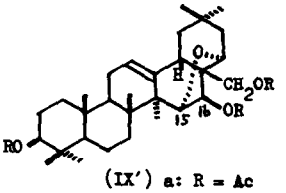
(XII)



(XI)



(I′)



(IX′) a: R = Ac
b: R = H

The arguments in favor of our conclusion, leading to the structures I having $C_{21}\beta$-OH and $C_{22}\alpha$-OH (trans diequatorial, provided that ring E is in a chair form) and IXb, are mostly based on the NMR analyses. Assuming that ring E of barringtogenol C has a boat or a twist boat conformation, its structure proposed by Barua and Chakrabarti[5] could be approved for theasapogenol B. Since the dihedral angle between $C_{21}\beta$-H and $C_{22}\alpha$-H in ring E boat conformation becomes close to 180°*, the coupling constant (J=10 cps.) for the protons on the α-glycolic carbons obtained in II or III appears reasonable by the structure with $C_{21}\alpha$-OH and $C_{22}\beta$-OH. However we prefer IXb for anhydrotheasapogenol B in view of the NMR analysis of IXa (two singlets at τ 6.39 (C_{21}-H), and τ 4.71 (C_{22} β-H)), and hence I for theasapogenol B (with the trans diequatorial glycol). The mechanistic consideration of its formation from II (see the footnote in the preceding page) would also support β-OH configuration at C_{21} rather than $C_{21}\alpha$-OH.

Studies concerning these hydroxylic configurations including ring E conformation of these related compounds are now in progress in this laboratory and will be published in a future paper.

We would like to express our deep thankness to Res. Lab. of Takeda Chemical Industries for measuring mass spectra, and to Dr. Barua of Bose Inst., Calcutta, India, for his generous gift of barringtogenol D triacetate.

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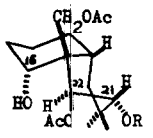
* 

R = H or R = Ac.