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THE STRUCTURES OF AESCIGENIN AND PROTOAESCIGENIN IN RELATION TO THEASAPOGENOLS A AND B (=BARRINGTOGENOL C): ON THE CONFIGURATION OF HYDROXYL GROUPS IN RING E*

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In previous papers, we have assigned the structures I and II both having 21β,22α-glycolic functions for theasapogenols A[1)*] and B[2)*] (Chart 1) which were isolated from the seeds saponin of Thea sinensis L. As mentioned there, the respective identities of theasapogenol B and anhydrotheasapogenol B (IIIa) with barringtogenol C (=aescinidin) and barringtogenol D, which have already been proposed by the previous workers as having 21α,22β-glycol (IV) and 22β-OH function (V) (Chart 2.), have disclosed the inconsistency concerned to the hydroxyl configurations in rings E of these compounds. The chemical structures of barringtogenol C (IV) and D (V) proposed by Barua et al.[3,4] were closely related to aescigenin (VI)[5], protoaescigenin (VII)[6], and isoaescigenin (VIII)[7], in particular barringtogenol D was directly linked to aescigenin by converting it to the common derivative (IX) (Chart 2). In the other words, these compounds have been believed to possess the identical hydroxyl configurations in rings E. Therefore, it is pertinent to reinvestigate on these points by use of aescigenin and protoaescigenin to shed light on the ambiguities. The present communication is toward the additional solution of these problems, using aescigenin and protoaescigenin, obtained from the seeds saponin of Aesculus turbinata Blume[8] (Japanese name, "Tochi-no-ki").

On acetylation with Ac_2O-pyridine at reflux for 50 min., protoaescigenin (X) afforded a pentaacetate (XII), mp. 205-211°, and a tetraacetate (XIII)**, mp. 238-242°. On dehydration of the pentaacetate with $SOCl_2$-pyridine mixture, it furnished an anhydro derivative, mp. 272-273°, $[\alpha]_D$ +10° (c, 0.7 in $CHCl_3$), whose structure should be expressed by XIVb in analogy of theasapogenol A, since the pentaacetate of the latter similarly yielded a Δ^{15}-16-desoxy derivative (XV). In view of the coupling

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** The free hydroxyl location at C_{21} was estimated analogously as in the case of theasapogenol A[1)].

constants (J=10~11 cps.) given in Table 1, all four derivatives possess the trans-diaxial vicinal hydrogens at C_{21} and C_{22}, which are in good accord with the NMR data reported in the previous studies

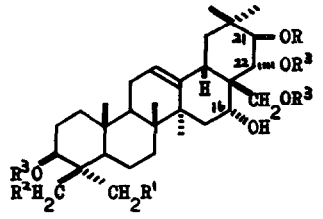
Table 1. (in τ -values, at 100 Mc.)

	XII	XIII	XIVb	XV(at 60 Mc.)
HC(21)-OR	R=Ac	R=H	R=Ac	R=Ac
HC(22)-OAc	4.58 4.70 (AB q., J=10 cps.)	6.09(d.) 4.86(d.) J=10 cps.	4.68 5.28 (AB q., J=11 cps.)	4.57 5.17 (AB q., J=10 cps.)

on theasapogenols A[1] and B[2]. On the other hand, Thomson proposed VIII[7] for isoaescigenin, which he prepared by the acidic treatment of either aescigenin or protoaescigenin. The structure VIII corresponds to the merely dehydrated product of VII, proposed structure of protoaescigenin by Jeger et al.[5], and should also be applicable to Δ^{15}-16-desoxy derivative of protoaescigenin (XIVa) prepared by us. However, the physical data comparison of both compounds showed that they were clearly not identical. According to Thomson, isoaescigenin pentaacetate exhibited the signals of two vicinal protons on the glycolic carbons at τ 5.04(d.) and 4.68(d.) with a small coupling constant (J=2.8 cps.) in its NMR spectrum, suggesting both hydrogens could be situated either in an equatorial-equatorial or in an equatorial-axial correlation. Considering from the formation mechanism of isoaescigenin from aescigenin as indicated by Thomson(partial stereostructure i in Chart 2), isoaescigenin must carry a 21α-OH group. As the hydroxyl configurations at C_{22} of isoaescigenin and Δ^{15}-16-desoxy-protoaescigenin are identical, both of the compounds must be epimeric at C_{21}. It follows that Δ^{15}-16-desoxy-protoaescigenin should possess 21β-OH function and in addition it must have 22α-OH as estimated above by the coupling constant (J=11 cps.) due to the trans-diaxial vicinal protons on C_{21} and C_{22}(XIVb in Table 1). Isoaescigenin is consequently best represented by XVI, having 21α,22α-glycol (axial-equatorial) configuration. The NMR evidence of isoaescigenin given by Thomson[7] is fully consistent with XVI. Accordingly, protoaescigenin should be expressed by the structure X with 21β,22α-glycol (trans-diequatorial) rather than the previously presented VII*.

The decisive basis for Jeger et al.[5] to assign 22β-OH configuration in aescigenin (as VI) lies mostly on the metal hydride reduction of the ketonic compound (XVII) yielding a 22-OH epimer (XVIII) as shown in Chart 2. They claimed the major product of the reduction to possess an equatorial (22α-OH) orientation. However, it should be noted that the metal hydride reduction in such a strained system

* The possibility, as mentioned in our previous paper,[2] of ring E boat or twist boat conformation in protoaescigenin with the structure (VII) can now be ruled out, since the coupling constant (J=2.8 cps.) of isoaescigenin given by Thomson could only be rationalized by the ring E chair conformation in VIII or XVI.



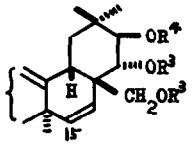
(I) R^1=OH, R^2,R^3,R^4=H theasapogenol A

(II) R^1,R^2,R^3,R^4=H theasapogenol B (=barringtogenol C, aescinidin)

(X) R^1,R^3,R^4=H, R^2=OH protoaescigenin

(XII) R^1=H, R^2=OAc, R^3,R^4=Ac

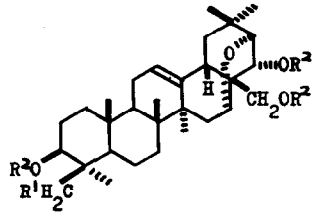
(XIII) R^1,R^4=H, R^2=OAc, R^3=Ac



(XIV) a: R^1,R^3,R^4=H, R^2=OH Δ^{15}-16-desoxy-protoaescigenin

b: R^1=H, R^2=OAc, R^3,R^4=Ac

(XV) R^1=OAc, R^2=H, R^3,R^4=Ac Δ^{15}-16-desoxy-theasapogenol A pentaacetate

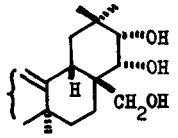


(III) a: R^1,R^2=H anhydrotheasapogenol B (=barringtogenol D)

b: R^1=H, R^2=Ac

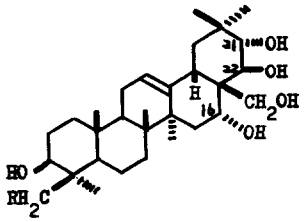
(XI) a: R^1=OH, R^2=H aescigenin

b: R^1=OAc, R^2=Ac



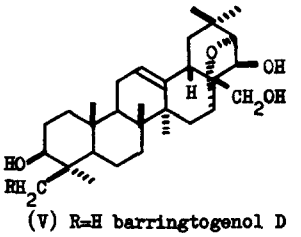
(XVI) R^1=OH, R^2=H isoaescigenin

Chart 1. Structures proposed by the present authors



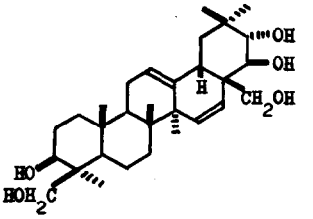
(IV) R=H barringtogenol C (=aescinidin)

(VII) R=OH protoaescigenin

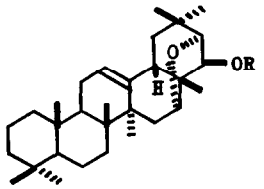


(V) R=H barringtogenol D

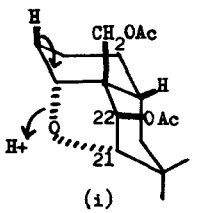
(VI) R=OH aescigenin



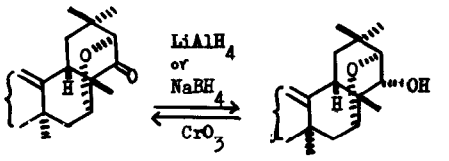
(VIII) isoaescigenin



(IX) R=H, Ac



(i)



(XVII) (XVIII)

Chart 2. Proposed structures by the previous workers[3,4,5,6,7]

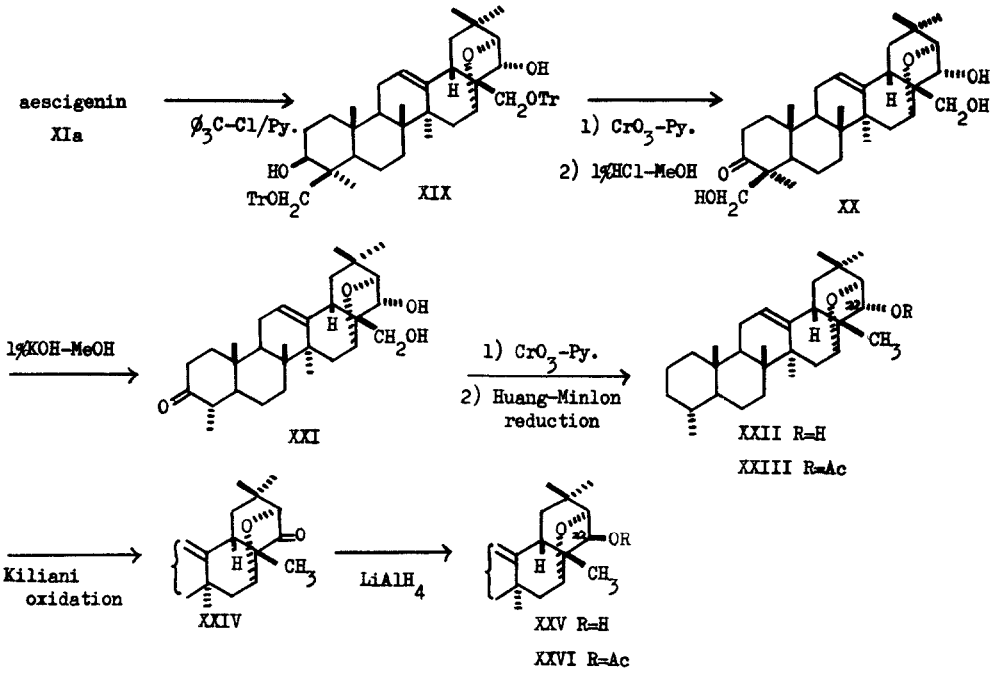


Chart 3.

as XVII could not necessarily yield a thermodynamically stable equatorial isomer, and the further proof has been needed for assigning the derived hydroxyl group especially when lacking the suitable example. We prepared an acetate (XXIII), a ketone (XXIV), and an epimeric acetate (XXVI) starting from aescigenin through the modified procedure of the method originally described by Jeger et al.[5] (Chart 3). The NMR analyses of XXIII and XXVI revealed that the former has 22α-OAc group and the latter epimer, on the contrary, possesses 22β-OAc based on their signal patterns (no coupling in XXIII, whereas a doublet with J=6 cps. in XXVI) due to the protons attached to the carbons bearing acetoxyl groups (Table 2). The Dreiding model inspection corroborates the above assignment by the fact that the dihedral angle between 21-H and 22β-H in XXIII is ca. 90°, while the angle of 21-H and 22α-H in XXVI is ca. 30°. The similar assignments are true in the NMR spectra of aescigenin tetraacetate (XIb) and anhydrotheasapogenol B triacetate (IIIb)[2], exhibiting singlets at τ 4.80 and 4.71 due to the protons at C_{22} respectively (Table 2). The results led us to revise the structure of aescigenin from VI to XIa, and consequently the structures of barringtogenol C (=aescinidin) and D must be expressed by II and IIIa respectively.

The discussions postulated here are in good agreement with the results previously obtained in theasapogenols A[1] and B.[2]

Table 2. (in τ -values, at 100 Mc.)

	XXIII	XXVI		XIb	IIIb(at 60 Mc.)
C(21)-H	6.53 (s.)	6.33 (d.)	* J=6 cps.	6.49 (s.)	6.39 (s.)
H-C(22)-OAc	4.97 (s.)	5.09 (d.)		4.80 (s.)	4.71 (s.)
C(16)-H	5.92 (m.)	6.30 (m.)		5.82 (m.)	5.71 (m.)

* The chemical shift and its coupling pattern were determined by decoupling experiment.

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