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THE CONSTITUTION OF SWIETENINE,
A NOVEL TETRANORTRITERPENOID.

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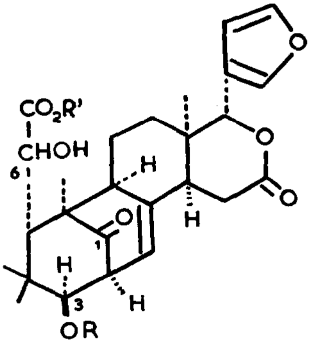
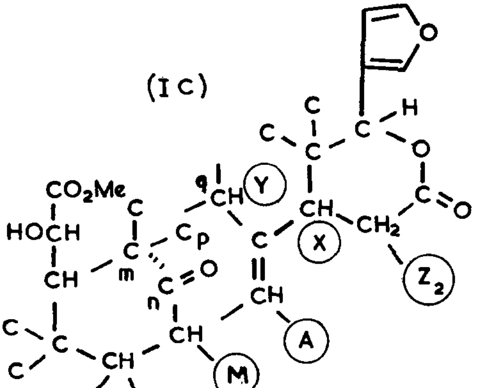
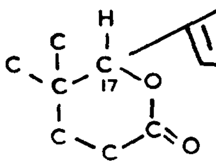
Swietenine, isolated (1) from the seeds of <u>Swietenia macrophylla</u>, has been investigated (2) by Chakrabarthy and Chatterjee. Its constitution and stereochemistry have been established (3) as (I) by an X-ray investigation of the p-iodobenzoate (II) of destigloylswietenine. We summarise here the salient chemical and nuclear magnetic resonance data which lead to the part structure (IC) for swietenine.



(I) R=tigloyl; R' =Me
(II) R=p-COC$_6$H$_4$I; R' =Me
(IV) R=H; R' = H; 3-epi
(V) R=H; R' = Me; 3-epi
(VI) R=tigloyl; R' = Me; 3-epi
(VII) R=H; R' = Me



(IC)



(IA)

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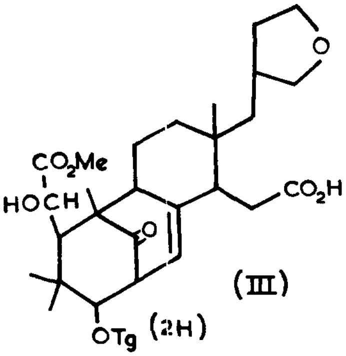
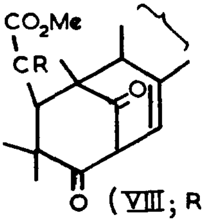
The composition, $C_{32}H_{42}O_9$, is established by the mass-spectrometric molecular weight of swietenine and two derivatives. Allowing for the functional groups contained in (I), which are completely defined by spectroscopic and chemical data, swietenine must be tricarbocyclic.

Catalytic reduction of swietenine affords an octahydro-acid (III) (not $\Delta^{\alpha\beta}$, α-OH or α-OR), m.p. 153-154°, $[\alpha]_D$ - 192° (methyl ester m.p. 164-165°, $[\alpha]_D$ - 179°) in which the isolated trisubstituted double bond survives, but the δ-lactone ($\nu_{max}^{CHCl_3}$ 1735 cm^{-1}) has been hydrogenolysed (H_{17}, sharp singlet at τ 4.3-4.6 present in all other derivatives, disappears), leading to part structure (IA).

Alkaline hydrolysis of swietenine gives the α-hydroxy acid (IV), m.p. 246-248°, $[\alpha]_D$ - 75°, pK 4.85, by retro- and realdolisation of the β-ketol system; this clearly cannot involve the hydroxyl of the α-hydroxy acid. Methylation and tigloylation give successively destigloyl 3-episwietenine (V) m.p. 243-246°, $[\alpha]_D$ - 67°, and 3-episwietenine (VI), m.p. 213-215°, $[\alpha]_D$ - 57°. Kupchan tiglate cleavage (4) of swietenine affords destigloyl swietenine (VII), m.p. 200-204°, $[\alpha]_D$ - 62°, which on oxidation gives the same triketone (VIII) m.p. 231-234°, $[\alpha]_D$ - 228°, as destigloyl 3-episwietenine (V). Oxidation of swietenine gives 6-dehydroswietenine (IX), m.p. 260-263, $[\alpha]_D$ - 149° (reconverted with sodium borohydride to swietenine) which on hydrolysis, methylation and oxidation leads to the same triketone (VIII). The 1,3-relationship of the

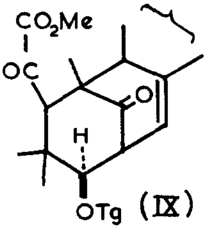


(III)



(VIII; R = O)

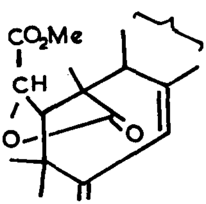
(X ; R = H,OH)



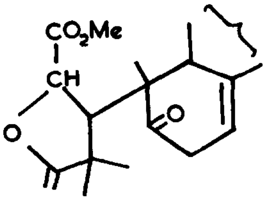
(IX)

ketonic and tiglate functions in swietenine, implied by alkali-induced epimerisation at C-3, is further supported as follows. Zinc reduction of the triketone (VIII), gives the diketone (X), m.p. 221-223°, $[\alpha]_D$ - 254°, and this with mild base undergoes β-dicarbonyl cleavage to a γ-lactonic ester, m.p. 259-263°, $[\alpha]_D$ + 113° $\nu_{max}^{CHCl_3}$ 1783, 1738, 1717 cm^{-1}. Failure of the double bond to conjugate with the carbonyl function suggests for this the cyclooctenone (XI) rather than the alternative cyclohexenone (XIa) structure.

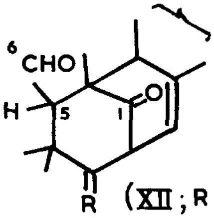
The α-hydroxy ester function in swietenine is related to the tiglate ester as follows. Oxidation with lead dioxide of the α-hydroxyacid (IV) affords the nor-aldehyde (XII), m.p. 233-236°, $[\alpha]_D$ - 47° [sharp doublet (J 6.5 c.p.s.) at τ 0.18; aldehydic H coupling with H_5 (τ 7.25), which couples with no other]. The aldehyde function resists normal oxidising conditions [CrO_3/acetic acid gives (XIII), m.p. 213-217°, $[\alpha]_D$ - 186°], but with



(XI)



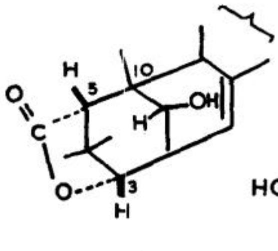
(XIa)



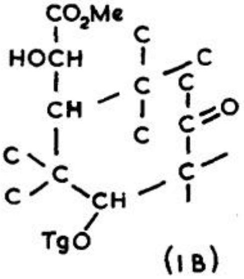
(XII; R = βH,αOH)
(XIII; R = O)

methanolic potassium hydroxide undergoes an intramolecular Cannizzaro reaction with the C-1 carbonyl to give the γ-lactone (XIV), m.p. 242-246°, $\nu_{max}^{CHCl_3}$ 1731, 1770 cm^{-1}. In this, the new carboxyl can lactonise only with the already present C-3 hydroxyl, which defines <u>its</u> configuration in destigloyl 3-episwietenine (V). The $^4J_{H_3H_5}$ coupling (5) (7 c.p.s.) in the γ-lactone supports its geometry. C-4 and C-10 do not bear hydrogen, since H_5 is a sharp doublet in the aldehyde (XII) and γ-lactone (XIV), collapsing to a sharp singlet when decoupled respectively from H_6 and H_3.

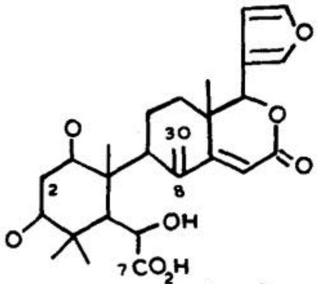
The part-structure (IB) which emerges at this point, can now be expanded to (IC) as follows.



(XIV)



(IB)



(XV)

The olefinic proton (A) [see (IC)] is spin-coupled to three others: (i) (M) [τ 7.1 in (V) and (XII) and τ 6.2 in (VIII) and (XIII); large coupling to (A) ($J = 6 - 8.5$ c.p.s.)]. (M) in turn couples with one other proton (N) [not otherwise coupled (except in the γ-lactone (XIV)); disappears in the 3-ketones] with a large coupling (11 c.p.s.) in swietenine, but small coupling (1 c.p.s.) in 3-episwietenine. (ii) (X) and (Y) [τ 7.4 - 8.0; small coupling to (A) ($J = 1 - 2$ c.p.s.)]. One, (X) or (Y), in turn couples with a methylene group (Z_2) [τ7.8 - 7.9; J = 2 - 4 c.p.s.] which is not otherwise coupled and from its position must be α to the δ-lactonic carbonyl.

Since both cyclic carbonyl groups in (VIII) and (XIII) are cyclohexanones, carbon atoms m and n (see IC) can be joined to form a 6-ring. Carbon atoms p and q are very probably identical since this then leaves two carbon atoms for construction of the third carbocyclic ring. This leads to a bicyclo [2:2:1]nonenone, which accounts for (a) non-conjugation of the isolated double bond with either carbonyl function at C-1 or C-3 and (b) non enolisation of the β-diketones (VIII) and (XIII).

The carbon skeleton of swietenine is readily derived by Michael addition of C-2 to C-30 in a precursor of type (XV) and represents the first example of C-7/C-8 cleavage in a tetranortriterpenoid.

REFERENCES

1. S.S.G. Sircar and T. Chakrabarthy, J. Ind. Chem. Soc., **28**, 207 (1951).
2. T. Chakrabarthy and A. Chatterjee, J. Ind. Chem. Soc., **32**, 179 (1955); idem, ibid., **34**, 117 (1957); S. Ghosh, T. Chakrabarthy and A. Chatterjee, ibid., **37**, 440 (1960).
3. A.T. McPhail and G.A. Sim, following communication.
4. S.M. Kupchan, A.D.J. Balon and E. Fujita, J. Org. Chem., **27**, 3103 (1962).
5. A. Rassat, C.W. Jefford, J.M. Lehn and B. Waegell, Tetrahedron Letters, **5**, 233 (1964).