1281. *Tetranortriterpenoids. Part I.* [*Bicyclononanolides. Part I.*] *The Constitution of Swietenine* [1]

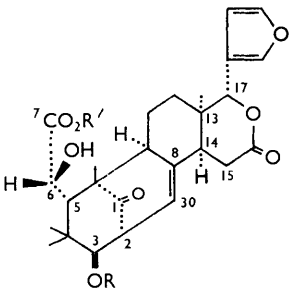
By J. D. Connolly, R. Henderson, R. McCrindle, K. H. Overton, and N. S. Bhacca

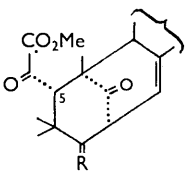
Correlation of the chemical and spectroscopic properties of swietenine and a number of its transformation products leads to the part-expression (Ic) for swietenine. The complete constitution and stereochemistry (I), established by an *X*-ray investigation of the *p*-iodobenzoate (II), reveal swietenine as the first member of a new group of terpenoid lactones, containing a bicyclo-[3,3,1]nonane nucleus, derivable through a hypothetical intermediate such as (XXI). The ready conversion of this system into a bicyclo[3,2,1]octane derivative is exemplified by transformation of the aldehyde (VI) into the γ-lactone (XVI).

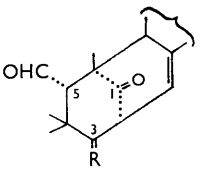
From the seeds of *Swietenia macrophylla* King (*Meliaceae*), a mahogany tree native to Central America and valued for its timber, Guha Sircar and Chakrabartty isolated [2] in 1951 two crystalline substances, one non-bitter which they named swietenine, the other bitter, named swietenolide. Of these only swietenine was characterised by the Indian workers; its chemistry is the subject of three subsequent publications [3-5] by Chakrabartty and Chatterjee.

Our interest in the chemistry of *Swietenia* constituents was first aroused by Drs. P. Schwarz and T. Chakrabartty of the University of Edinburgh, to whom we express our warm appreciation. In the present Paper we discuss the constitution and stereochemistry of swietenine (I).* Swietenolide will form the subject of a subsequent publication.

The constitution and stereochemistry of swietenine (I) have been established by an *X*-ray investigation [6] of the *p*-iodobenzoate (II) of detigloylswietenine. We here present the chemical and spectroscopic evidence which leads to part structure (Ic) for swietenine.







(I) R = Tigloyl; R′ = Me
(II) R = *p*-COC_6H_4I; R′ = Me
(IV) R = H; R′ = Me
(VIII) R = R′ = H; 3-epi
(IX) R = H; R′ = Me; 3-epi
(X) R = Tigloyl; R′ = Me; 3-epi
(VIIc) R = Dihydrotigloyl; R′ = Me

(V) R = β-Tigloyloxy, α-H
(XII) R = O
(XIII) R = β-OH, α-H
(XIV) R = α-OH, β-H

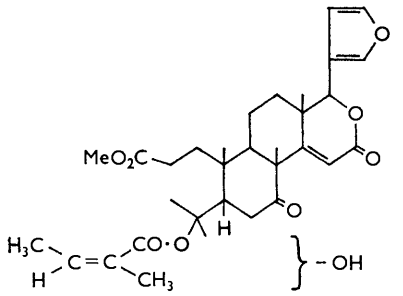
(VI) R = α-OH, β-H
(VIa) R = α-OAc, β-H
(XV) R = O

The following functional groups had been inferred correctly by the Indian workers when we began our study: (*a*) a β-substituted furan ring (u.v., i.r., and n.m.r.); (*b*) a

* For ease of exposition full structural formulæ anticipate their derivation where appropriate.

[1] Preliminary communication: J. D. Connolly, R. Henderson, R. McCrindle, K. H. Overton, and N. S. Bhacca, *Tetrahedron Letters*, 1964, 2593.
[2] S. S. G. Guha Sircar and T. Chakrabartty, *J. Indian Chem. Soc.*, 1951, **28**, 207.
[3] T. Chakrabartty and A. Chatterjee, *J. Indian Chem. Soc.*, 1955, **32**, 179.
[4] T. Chakrabartty and A. Chatterjee, *J. Indian Chem. Soc.*, 1957, **34**, 117.
[5] S. Ghosh, T. Chakrabartty, and A. Chatterjee, *J. Indian Chem. Soc.*, 1960, **37**, 440.
[6] A. T. McPhail and G. A. Sim, *Tetrahedron Letters*, 1964, 2599.

methoxycarbonyl group (unsupported by evidence); (*c*) a tiglate ester (formation of tiglic acid during hydrolysis). On the basis of the revised molecular formula $C_{32}H_{42}O_9$, certain other data partly contained in their earlier Papers, and (mainly) an assumed analogy with limonin,[7] Gosh, Chakrabartty, and Chatterjee later proposed [5] for swietenine the structure (III).



(III)

In our hands pure swietenine obtained by the procedure outlined in the Experimental section had m. p. 272—276° and rotatory dispersion in chloroform; $[\phi]_{600}$ −886, $[\phi]_{589}$ −948, $[\phi]_{312\cdot5}$ −12,810, $[\phi]_{275}$ +364°. The composition $C_{32}H_{40}O_9$ is established by the mass-spectrometric molecular weight of swietenine (568) and supported by the combustion analyses of over thirty derivatives.

The evidence concerning the functional groups can be summarised as follows. A β-substituted furan ring is indicated by the infrared (i.r.) $\nu_{max.}$ (Nujol) 3160w, 1505w, and 877s cm.$^{-1}$, and nuclear magnetic resonance (n.m.r.) (τ 2·43 and 2·56, 2αH, multiplets; τ 3·61, 1βH, diffuse singlet) spectra. Evidence for the secondary tiglate ester comes from the n.m.r. spectrum [τ 8·2 and 8·3, 6H, multiplet characteristic of tiglate vinyl methyl groups and τ 3·1, 1H, very broad multiplet characteristic of tiglate vinyl proton; τ 5·36, 1H, doublet (J = 11 c./sec.) of secondary tiglate ester which disappears in detigloylswietenine (IV)]. Furthermore, alkaline hydrolysis affords tiglic acid, characterised as the *p*-bromophenacyl ester. The grouping $CHOH{\cdot}CO_2Me$ gives rise in the n.m.r. spectrum to signals at τ 5·46 (1H, broad singlet) which disappears in dehydroswietenine (V) * and τ 6·23 (3H, singlet) and in the i.r. ($CHCl_3$) to bands at 3610 (free OH) and 3546 (bonded OH) cm.$^{-1}$. Moreover, hydrolysis affords an α-hydroxy-acid of typically low pK_a (4·85) which is oxidised by lead tetra-acetate or lead dioxide to a nor-aldehyde (see below). Two further oxygens are contained in a δ-lactone function, as evidenced for example by the i.r. spectrum of the nor-aldehyde (VI), $\nu_{max.}$ (CCl_4) 1752 cm.$^{-1}$, and the remaining oxygen in a cyclohexanone which resists, *inter al.*, oximation and reduction with sodium borohydride, but is apparent in the i.r. spectrum of swietenine [$\nu_{max.}$ (CCl_4) 1716 cm.$^{-1}$] and its rotatory dispersion (10^{-2} a = 90). One further double-bond equivalent resides in a trisubstituted olefinic linkage (τ 4·63, 1H multiplet; vinyl proton), which resists normal hydrogenating conditions (see below).

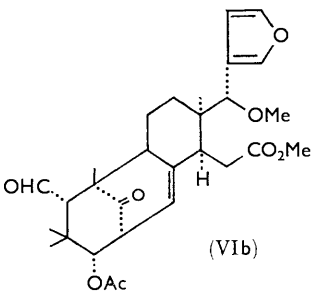
When allowance has been made for the functional groups indicated, swietenine, $C_{32}H_{40}O_9$, must be tricarbocyclic. Moreover, the residue, $C_{26}H_{32}O_8$, left when the contributions from one tiglate and one methyl ester have been subtracted, together with the presence in swietenine of a β-substituted furan ring, strongly suggests a kinship with limonin,[7] as already noted by the Indian workers. In addition, the fact that swietenine quite clearly according to its n.m.r. spectrum contains only four *C*-methyl and no vinyl methyl groups (the tiglate ester apart), must mean that the fifth nuclear methyl group of a euphol-type precursor, if such is to be assumed,[7] must be either oxidised (as in limonin) or more probably concealed in the formation of a new carbocyclic ring. We now consider in detail those aspects of the chemistry of swietenine which permit inter-relation of its

* The designation " dehydro " refers to the 6-dehydro-series.

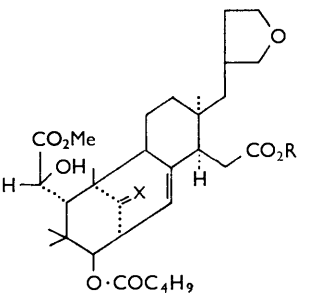
[7] D. Arigoni, D. H. R. Barton, E. J. Corey, O. Jeger, and collaborators, *Experientia*, 1960, **16**, 41.

functional groups and, with the aid of n.m.r. spectroscopy, derivation of the part-structure (Ic).

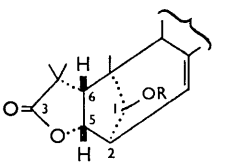
The most easily interpreted reaction of swietenine is its reduction in acetic acid over a palladium–charcoal catalyst, furnishing in >80% yield the octahydro-acid monomethyl ester $C_{32}H_{48}O_9$ (VII), m. p. 153—154°, $[\alpha]_D$ −190° [dimethyl ester (VIIa), $C_{33}H_{50}O_9$, m. p. 164—165°, $[\alpha]_D$ −179°]. This reaction is entirely analogous to the formation of hexahydrolimoninic acid [8] and the octahydrocolumbinic acids [9] and implies that the δ-lactone system of swietenine is attached allylically with respect to the furan ring, as indicated in the part-structure (Ia). As expected, the signals in the n.m.r. spectrum of swietenine attributable to the furanic protons (see above) and the proton at C-17 (τ 4·43) have disappeared in this compound. The fact that the C-17 proton appears as a sharp singlet in all derivatives which retain the δ-lactone ring makes it very probable that C-13 does not bear hydrogen. Survival in the octahydro-acid of an isolated double bond is evidenced by a positive tetranitromethane reaction, a vinyl proton signal in the n.m.r. spectrum (τ 4·46, 1H, multiplet), and end-absorption in the ultraviolet ($\lambda_{max.}$ 202 mμ, ε 6300). The surviving double bond resists osmylation. On the other hand the octahydro-diester (VIIa), unlike swietenine, was readily converted into a crystalline oxime (VIIb), m. p. 251—254°. Dihydroswietenine $C_{32}H_{42}O_9$ (VIIc), m. p. 224—229°, was readily prepared by hydrogenating swietenine in ethyl acetate over platinum oxide. Its n.m.r. spectrum indicates that the tiglate double bond has been saturated.



(VIb)



(VII) R = H; X = O
(VIIa) R = Me; X = O
(VIIb) R = Me; X = NOH



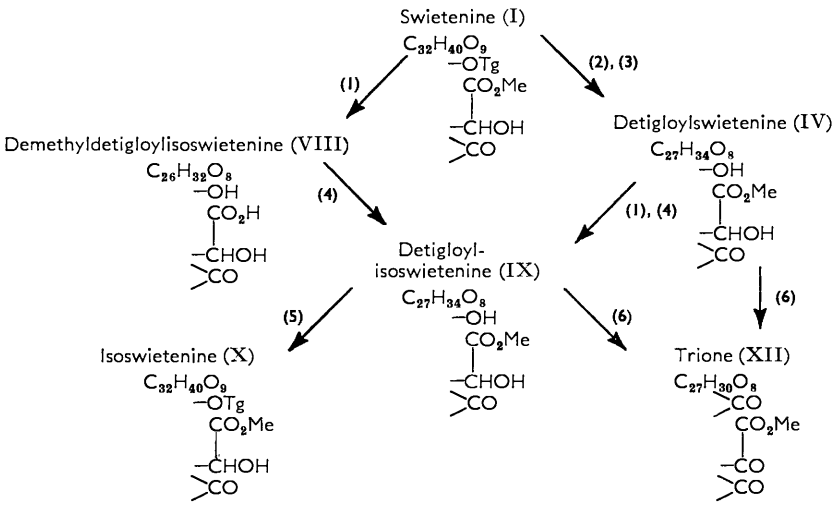
(XVI) R = H
(XVIa) R = Ac
(XVII) 1-dehydro- (XVI)
(XIX) 1-epi- (XVI)

The degradational sequence which we have employed in deriving the constitution of swietenine has as its first step the hydrolytic removal of the methyl and tiglate ester functions by alkali. Alkaline hydrolysis of swietenine in fact leads to a complex mixture of acidic products, thin-layer chromatography after methylation showing the presence of at least nine components. However, from this mixture there was isolated, by virtue of its insolubility in chloroform, demethyldetigloylisoswietenine (VIII),* $C_{26}H_{32}O_8$, m. p. 249—251°, $[\alpha]_D$ −75°, pK_a 4·85, as the major product in a maximum yield of 30%. It soon became evident that, in the formation of this substance, ester hydrolysis was accompanied by an additional, less obvious, change, for restoration of the ester functions by successive treatment with diazomethane and then tigloyl chloride in pyridine generated first detigloylisoswietenine (IX), $C_{27}H_{34}O_8$, m. p. 243—246°, $[\alpha]_D$ −67°, but then, instead of swietenine, an isomer (X), m. p. 213—215°, $[\alpha]_D$ −57°, possessing according to its i.r. and n.m.r. spectra the same functional groups as swietenine. It was essential to establish the precise nature of this concealed change since, were this to remain unresolved, the conclusions derived from subsequent transformations could not be invoked to deduce the structure of

* The designation " iso " refers to the 3-epi-series.

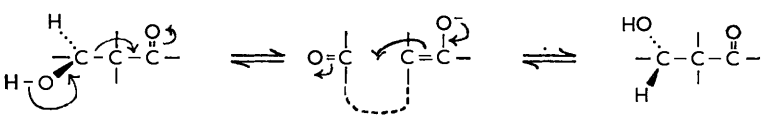
[8] O. H. Emerson, *J. Amer. Chem. Soc.*, 1952, **74**, 688.
[9] K. H. Overton, N. G. Weir, and A. Wylie, *Proc. Chem. Soc.*, 1961, 211.

swietenine. The problem was more narrowly defined as follows. Removal of the tiglate ester not by alkaline hydrolysis but by the procedure of Kupchan,[10] namely osmylation followed by periodate oxidation, afforded detigloylswietenine (IV), m. p. 200—204°, $[\alpha]_D$ −62°, isomeric with the detigloylisoswietenine obtained above. Detigloylswietenine was smoothly converted into its isomer by successive reaction with base and diazomethane, and both compounds afforded with the Sarrett reagent the *same* trione (XII), $C_{27}H_{30}O_8$, m. p. 231—234°, $[\alpha]_D$ −228°. These changes are summarised in Scheme 1. The additional change then occurs during conversion of detigloylswietenine into detigloylisowietenine. Taking into account that there is no change in the functional groups, three simple interpretations can be considered: (i) epimerisation α to the ketonic (or ester) carbonyl function; (ii) intramolecular (or conceivably intermolecular) hydride transfer between the ketone and hydroxyl functions, resulting in their positional interchange, or (iii) dealdolisation and re-aldolisation, involving the hydroxyl and ketonic functions and resulting in epimerisation at the carbinol carbon atom (see Scheme 2). We favoured the third alternative, since the rotary dispersion and circular dichroism curves of the pairs swietenine and isoswietenine and the corresponding detigloyl derivatives (see Experimental section), differ only in amplitude but not in the sign or positions of their extrema. It seemed very probable that the relationships implied in alternatives (i) and (ii) would be reflected in more strikingly different optical properties. That the α-hydroxy-ester hydroxyl group does not participate in the de- and re-aldolisation sequence, and that it (or the neighbouring C-5) is not



Reagents: (1) KOH–MeOH; (2) OsO_4; (3) HIO_4; (4) CH_2N_2; (5) TgCl–C_6H_5N; (6) CrO_3–C_6H_5N; [Tg = $COC(CH_3)=CH(CH_3)$].
Only the functional groups shown are affected during these transformations.

Scheme 1



Scheme 2

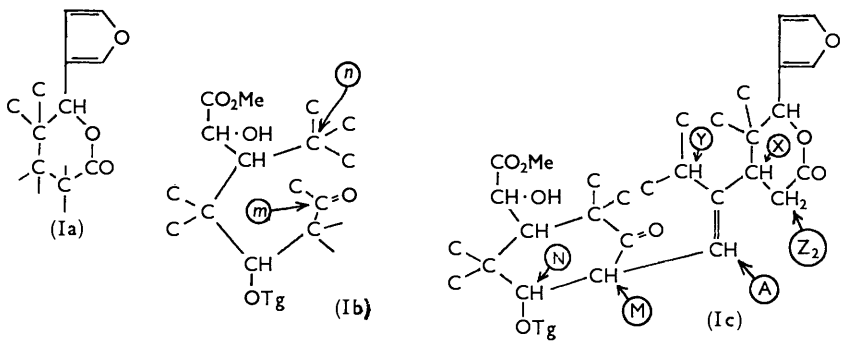
epimerised by an oxidation–reduction process could be demonstrated as follows: Sarrett or Jones oxidation of swietenine affords the α-oxo-ester, dehydroswietenine (V), $C_{32}H_{38}O_9$, m. p. 261—265°, $[\alpha]_D$ −149° (which was stereoselectively reconverted into swietenine with sodium borohydride or zinc in acetic acid). This shows in its n.m.r. spectrum disappearance of the C-6 proton at τ 5·46 in swietenine and the paramagnetic shift (and very marked

[10] S. M. Kupchan, A. D. J. Balon, and E. Fujita, *J. Org. Chem.*, 1962, **27**, 3101.

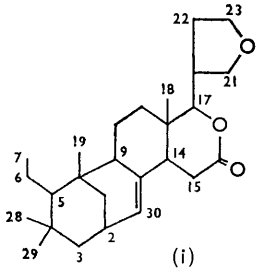
sharpening) of the C-5 proton from the already abnormally low value of τ 6·49 in swietenine to τ 4·97 in dehydroswietenine. Kupchan tiglate cleavage [10] of the latter gave dehydrodetigloylswietenine (XIII), $C_{27}H_{32}O_8$, m. p. 210—214°, $[\alpha]_D$ −54°, which, on alkaline hydrolysis and remethylation led to dehydrodetigloylisoswietenine (XIV), m. p. 242—246°, $[\alpha]_D$ −74°, obtainable direct from dehydroswietenine by hydrolysis and remethylation. Both hydroxy-diones were oxidised to the trione (XII) previously obtained from detigloylswietenine and detigloylisoswietenine. Borohydride reduction of dehydrodetigloylswietenine to detigloylswietenine showed that epimerisation at C-5 had not occurred.

The conclusion emerges that the change from detigloylswietenine to detigloylisoswietenine proceeds through mechanism (iii), involving the ketonic carbonyl group and the secondary hydroxyl group that is tigloylated in swietenine, and results in epimerisation of the latter showing that these functions must bear a 1,3-relationship one to the other. This conclusion is borne out by the change in the coupling constant between the proton (N) and its only neighbour (M) (see Ic) from 11 c./sec. in swietenine to 2 c./sec. in isoswietenine, where the effect is more clearly evident than in the corresponding alcohols. Three other changes are striking in comparing the n.m.r. spectra of detigloylswietenine and detigloylisoswietenine: (i) a paramagnetic shift of the vinyl proton (A) from τ 4·30 to τ 4·08; (ii) a diamagnetic shift of proton (M) from τ 6·5 to τ 7·12; and (iii) a paramagnetic shift of one C-methyl group from τ 9·12 to τ 9·0. These observations are satisfactorily accommodated by reference to the complete structures of these compounds. We have encountered in a number of swietenine derivatives the base-promoted fission of the C-2—C-3 bond, either by β-dicarbonyl cleavage of a 1,3-dione or dealdolisation of a 1,3-ketol system, which lead to an array of interesting products (to be discussed in a forthcoming publication).

We next consider the relationship of the α-hydroxy-ester and tiglate functions. As previously indicated, alkaline hydrolysis of swietenine leads to demethyldetigloylisoswietenine (VIII). Oxidation of this α-hydroxy-acid with either lead tetra-acetate in acetic acid at 20° or with lead dioxide in refluxing acetic acid, led to a noraldehyde (VI), $C_{25}H_{30}O_6$, m. p. 234—237°, $[\alpha]_D$ −47° [acetate (VIa), m. p. 274—279°, $[\alpha]_D$ −34°]. The aldehydic proton at τ 0·18 is cleanly coupled (J = 6 c./sec.) with a single neighbour (τ 7·25) at C-5, which in turn is only very feebly coupled ($J \leqslant 0{\cdot}5$ c./sec.; ^4J coupling with H-3?), suggesting that the carbon atoms flanking C-5 do not bear hydrogen. This is supported by the fact that in dehydroswietenine (V), H-5 (τ 4·97) appears as a sharp singlet. The aldehyde function resists oxidation under normal conditions. Thus, chromium trioxide in either acetic acid or pyridine furnished the dioxo-aldehyde (XV), $C_{25}H_{28}O_6$, m. p. 218—221°, $[\alpha]_D$ −193°. On the other hand reaction of the hydroxy-oxo-aldehyde (VI) with



0·25N-sodium hydroxide in aqueous ethanol (1 : 1) at 95° afforded an isomeric γ-lactone (XVI), m. p. 242—246°, $[\alpha]_D$ +111° [$\nu_{max.}$ ($CHCl_3$) 1770 (γ-lactone), 1732 (δ-lactone), 3620, 3587 cm.$^{-1}$ (unbonded and bonded OH)]. We return later to the genesis of this γ-lactone. The following simplified analysis is sufficient at this stage in the argument. If one accepts

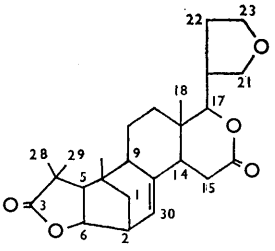


(i)

Chemical shifts (τ) and coupling constants * (c./sec. in parentheses) of protons in swietenine and its derivatives

Position of protons [see formulæ (i) and (ii)]

	30	2	3	5	6	9	14	15	17	21 23	22	18 19	28 29	7 CO_2Me
(I)	4·63	6·50	5·36	6·49	5·46	7·78		7·24	4·43	2·43	3·61	8·57	9·03	6·25
	(7, 2)	(7, 11)	(11)			(1, 2)		(4)		2·56		8·88	9·12	
(IV)	4·30	6·5	6·5	6·62	5·43	7·7		7·07	4·32	2·45	3·58	8·57	9·01	6·29
										2·53		8·99	9·12	
(V)	4·55	6·4	5·08	4·97	—	7·77		7·15	4·32	2·27	3·55	8·80	8·99	6·01
	(7, 1)	(7, 9)	(9)					(4)		2·57		8·93	9·08	
(VI)	4·13	7·06	6·26	7·25	0·18	7·68		7·1	4·60	2·34	3·53	8·63	8·92	—
	(7)	(7, 1)	(1)	(6)	(6)	(4)		(4)		2·56		8·87	8·95	
(VIa)	4·02	7·11	5·35	7·1	0·14	7·7		7·05	4·55	2·31	3·48	8·62	8·92	—
										2·51		8·80	9·01	
(VIb)	4·12	6·98	5·29	6·98	0·23	7·7		7·12	5·76	2·20	3·51	8·59	8·93	—
										2·53		8·74	8·98	
(VIIa)	4·46	6·8	5·46	6·68	5·53	7·7		7·63	—	—	—	8·68	9·09	6·40
												8·91	9·17	6·19
(VIIc)	4·46	6·50	5·22	6·46	5·36	7·8		7·2	4·32	2·45	3·54	8·76	8·95	6·46
										2·56		8·84	9·07	
(IX)	4·08	7·12	?	6·37	5·43	7·74		7·10	4·44	2·56	3·63	8·55	9·0	6·27
	(8, 2)	(8)		(1·5)	(1·5)	(2)				2·45		9·0	9·0	
(X)	3·88	7·10	5·24	6·63	5·34	7·62		6·98	4·33	2·43	3·54	8·44	8·96	6·16
										2·53		8·76	8·96	
(XII)	4·25	6·2?	—	5·32	—	7·7		7·08	4·50	2·32	3·47	8·72	8·91	6·07
	(7, 2)	(7)				(4)				2·57		8·86	9·00	
(XIII)	4·25	7·25	?	5·17	—	7·8		7·05	4·28	2·30	3·52	8·80	9·03	6·09
										2·52		8·92	9·10	
(XIV)	4·08	7·1	6·15	5·58	—	7·3	7·68	7·10	4·37	2·32	3·57	8·76	8·92	6·08
							(4)	(4)		2·57		8·97	9·12	
(XV)	4·32	6·22	—	7·0	0·13	7·50	7·65	7·1	4·73	2·36	3·53	8·58	8·75	—
	(7, 2)	(7, 1)		(5)	(5)	(1)	(4)	(4)		2·56		8·83	8·92	



(ii)

	30	2	1	5	6	9	14	15	17	21 23	22	18 19	28 28	3 CO_2Me
(XVIa)	4·45	6·88	5·04	7·48	5·33	7·68		7·10	4·78	2·58	3·62	8·61	8·79	—
	(8, 2)	(8, 5)	(5)	(7)	(7)	(4, 2)		(4)		2·58		8·66	8·94	
(XVII)	4·18	6·91	—	6·92?	5·08	7·6		7·15	4·58	2·48	3·55	8·60	8·73	—
										2·48		8·70	8·95	
(XVIIIa)	4·42	6·92	—	7·36	5·51	7·7		7·15	4·29	2·48	3·53	8·67	8·96	6·31
										2·50		8·82	9·04	

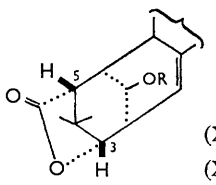
* Determined by double resonance at 100 Mc./sec.

Coupling constants used in the text which do not appear in this Table were inferred from spectra at 60 Mc./sec. by inspection.

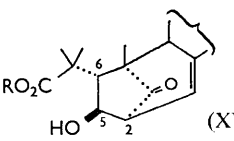
that the δ-lactone and furan ring of swietenine are unaffected during formation of the γ-lactone, and this appears to be justified by careful comparison of the n.m.r. spectra of the two compounds, then the only oxygen functions of the nor-aldehyde that need be considered during its transformation into the γ-lactone are the formyl group, the ketonic function present in swietenine, and the hydroxyl group which in swietenine is tigloylated. The conversion of these three functions into a hydroxy-γ-lactone suggests the intervention of an intramolecular Cannizzaro reaction. On the simplest interpretation this leads to the part-structure (Ib) for swietenine, with the proviso that the tiglate and ketone functions could be interchanged and/or carbon atoms *m* and *n* joined.

The part-structure (Ib) can be expanded by the application of nuclear magnetic double-resonance studies at 100 Mc/sec. as follows. The proton (M) (see Ic) at τ 6·50, situated between the tiglate ester and ketone in swietenine, is spin-coupled (J = 7 c./sec.) to the olefinic proton (A) at τ 4·63. A similar large coupling (6—8·5 c./sec.) is observed between the corresponding protons in, for instance the derivatives (IX), (V), (XII), (VI), and (XV) [see Table]. The olefinic proton (A) is moreover coupled with a small coupling (J = 1—2 c./sec.) to two allylic protons (X) and (Y) at τ 7·78, attached either to the same or to different carbon atoms. (X) or (Y) is in turn coupled to a methylene group (Z_2) at τ 7·24 (J = 4 c./sec.), which is not otherwise coupled and from its chemical shift must be α to the lactonic carbonyl group. The proton (M), in addition to its coupling with the vinylic proton (A), also interacts with one other, (N), situated at τ 5·36 (J = 11 c./sec.).

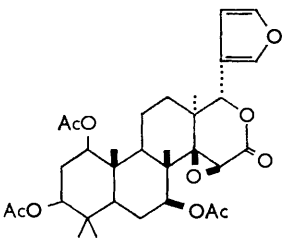
The sequence of functionality revealed by these data, when combined with part-structure (Ib), permits expansion to (Ic). Moreover, the n.m.r. data of a number of derivatives, assembled in the Table strongly support this proposal. The complete constitution and stereochemistry of swietenine (I), disclosed by the *X*-ray investigation,[6] can be readily rationalised in terms of the Biogenetic Isoprene Rule.[11] Fission of ring B between C-7



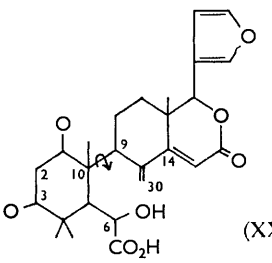
(XVIb: R = H)
(XVIc: R = Ac)



(XVIII: R = H)
(XVIIIa: R = Me)



(XX)



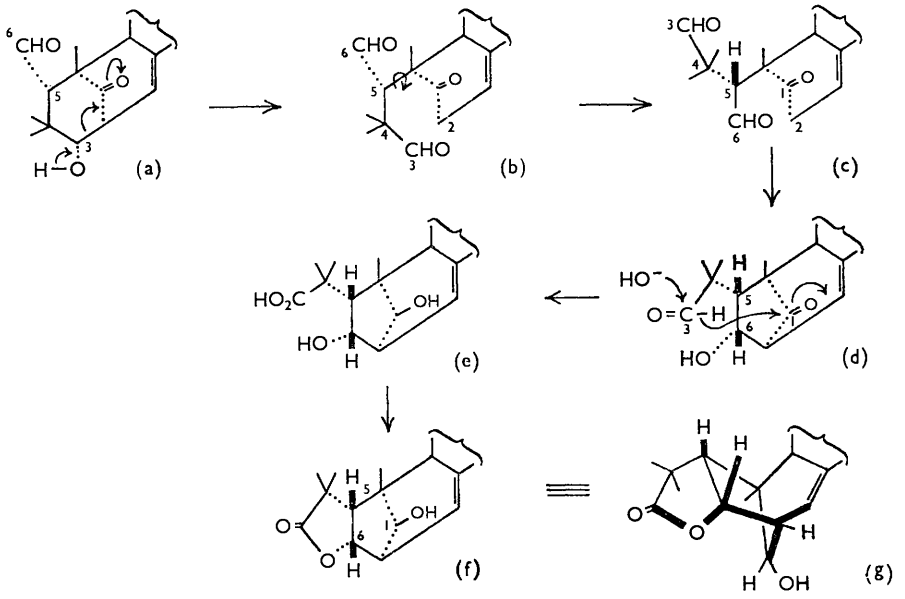
(XXI)

and C-8 of a precursor related to the natural khivorin (XX) [12] and additionally oxygenated at C-6, could lead to the intermediate diene-lactone (XXI). Rotation about C-9 and C-10 and intramolecular Michael addition of C-2 to C-30 would result in formation of the bicyclononanone system of swietenine. We are at present engaged in providing a laboratory analogy for this step. The configurations of all asymmetric centres except C-3, C-6, and C-14, which are the results of secondary processes, are consonant with the derivation of swietenine from a euphol-type precursor. A point which merits comment is the shift in swietenine of the isolated double bond from the position that would result from the proposed ring-closure, *i.e.*, 8(14) or 14(15), into the bicyclononane system at position 8(30).

[11] L. Ruzicka, *Pure Appl. Chem.*, 1963, **6**, 493, and references therein.
[12] C. W. L. Bevan, T. G. Halsall, M. N. Nwaji, and D. A. H. Taylor, *J.*, 1962, 768.

As we shall demonstrate in a subsequent Paper, swietenolide, which occurs in the same tree, and a third related substance, mexicanolide from *Cedrela mexicana*,[13] both have the isolated double bond in the expected 8(14)-position.

We now return to the γ-lactone, obtained from the noraldehyde (VI) by the action of alkali. This we formulated in a preliminary communication [1] as (XVIb), assuming that it arose from intramolecular Cannizzaro reaction between the aldehyde and ketone functions in (VI), and subsequent lactonisation of the new carboxyl with the hydroxyl group at C-3. (The hydroxyl at C-1, as a result of hydride transfer from the formyl group, is unsuitably oriented for lactonisation.) However, the n.m.r. spectrum of the derived acetate $C_{27}H_{32}O_7$, m. p. 274—278°, caused misgivings concerning its formulation as (XVIc). In particular, while the protons attached to " C-3 " (τ 5·33) and " C-5 " (τ 7·48), shown by double resonance to be mutually coupled, possessed on our original formulation the geometry required for ^4J coupling, the size of the coupling constant (7 c./sec.) was considerably larger than is normally observed in such circumstances [14] and caused us to reconsider our proposal. We now suggest for the γ-lactone the revised structure and stereochemistry (XVI),* which we visualise as being formed by the sequence indicated in Scheme 3. Two points deserve comment. Aldolisation between C-2 and C-6 [see (c)] to form (d) [rather than between C-2 and C-3 which would reform (a)], cannot occur until the configuration at C-5 [in (b)] has been inverted (models clearly show that prior to this change, steric crowding between C-4 and C-9 is too severe in the transition state required for C-2—C-6 bond formation).



Scheme 3

However, as soon as epimerisation at C-5 has taken place, hydride transfer between C-3 and C-1 becomes possible and must then displace successive equilibria towards the dihydroxy-acid (e). In the resulting lactone (f), the two mutually coupled protons (H-5

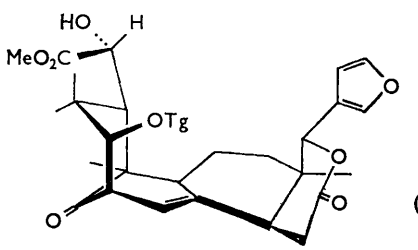
* It should be noted at once that the conclusions implied in the part-structure (Ib) are in no way invalidated by the reformulation of the γ-lactone. So long as the ketone in swietenine is contained in a six- rather than a five-membered ring, and this is patent in all the relevant i.r. spectra, the tiglate must be placed on the δ-carbon atom with respect to the methyl ester.

[13] J. D. Connolly, R. McCrindle, and K. H. Overton, *Chem. Comm.*, 1965, **8**, 162.

[14] A. Rassat, C. W. Jefford, J. M. Lehn, and B. Waegell, *Tetrahedron Letters*, 1964, 233; S. Sternhell, *Rev. Pure Appl. Chem. (Australia)*, 1964, **14**, 15.

and H-6) which occasioned our doubts are now vicinal and coplanar [see (g)] and this satisfactorily accounts for the magnitude of the observed coupling [15] in the n.m.r. spectrum of the acetate (XVIa). The observed couplings between H-1 (τ 5·04) and H-2 (τ 6·88) (J = 5 c./sec.) and between H-2 and H-6 (τ 5·33) (J = 1 c./sec.) are in accordance with the dihedral angles (θ = 45° and 90°, respectively) relating to these pairs of protons. Support for the newly formed bicyclo[3,2,1]octene system [as in (XVI)] comes from the oxidation product (XVII), $C_{25}H_{28}O_6$, m. p. 248—251°, $[\alpha]_D$ +190°, of the γ-lactone. This exhibits in its i.r. spectrum ($CHCl_3$), in addition to bands for the γ-lactone (1781) and δ-lactone (1735), a new carbonyl band at 1762 cm.$^{-1}$ characteristic [16] of the bridgehead carbonyl group in such a system. Exposure of the dehydro-γ-lactone (XVII) to the alkaline conditions required to bring about γ-lactone formation resulted, on acidification, in a mixture of two parts of a hydroxy-acid (XVIII), $C_{25}H_{32}O_7$, characterised as the methyl ester (XVIIIa), $C_{26}H_{34}O_7$, m. p. 209—212°, $[\alpha]_D$ +120°, and one part of recovered γ-lactone. Again, the magnitude of the coupling of H-5 in the ester (XVIIIa) with its two neighbours [J = 7 c./sec. with H-2 (θ ~20°) and 4·5 c./sec. with H-6 (θ ~115°)] supports the proposed epimerisation at C-6, which presumably occurs in this series, as in the bicyclo[3,3,1]nonene series, by de- and re-aldolisation. Reduction of the dehydro-γ-lactone with sodium borohydride regenerated the γ-lactone as the major product (more than 90%). The minor epimeric hydroxy-lactone (XIX), although non-crystalline, was homogeneous as judged by thin-layer chromatography, and showed interesting differences from its epimer in the i.r. region. Thus, while the original γ-lactone exhibited in chloroform only partial and weak hydrogen bonding in the hydroxyl region (3587sh cm.$^{-1}$) presumably attributable to interaction between the hydroxyl group and the isolated double bond, the 1-epi-γ-lactone showed very extensive hydrogen bonding in the same solvent (very broad band 3350—3550 cm.$^{-1}$), presumably resulting from strong interaction of the hydroxyl with the γ-lactone carbonyl, the frequency of which was lowered from 1783 in lactone (XVI) to 1758 cm.$^{-1}$ (CCl_4) in the 1-epi-lactone.

Swietenine is the first member of a sub-family of tetranortriterpenoids which contain a bicyclo[3,3,1]nonane nucleus, not previously encountered among natural isoprenoids. Since these compounds additionally contain a lactone function, we propose for them the generic name of bicyclononanolides. The conformation of the bicyclic nucleus as revealed



(XXII)

by the *X*-ray work [see (XXII)],[6] that of a boat–quasi-chair, contrasts with the chair–chair arrangement in simple bicyclo[3,3,1]nonanes [17] and is undoubtedly the result of non-bonded interactions among the numerous substituents which encumber the bicyclic nucleus.

At the time of our preliminary announcements of the structure of swietenine, two naturally occurring substances, closely related to the hypothetical intermediate (XXI) for swietenine, appeared. These are andirobin [18] and methyl angolensate,[19] and insofar

[15] M. Karplus, *J. Chem. Phys.*, 1959, **30**, 11; N. S. Bhacca and D. H. Williams, "Applications of NMR Spectroscopy in Organic Chemistry," Holden-Day, 1964, pp. 49—51.
[16] N. A. LeBel and L. A. Spurlock, *Tetrahedron*, 1964, **20**, 215.
[17] W. A. C. Brown, J. Martin, and G. A. Sim, *J.*, 1965, 1844.
[18] W. D. Ollis, A. D. Ward, and R. Zelnik, *Tetrahedron Letters*, 1964, 2607.
[19] C. W. L. Bevan, J. W. Powell, D. A. H. Taylor, P. Toft, H. Welford, W. R. Chan, B. S. Mooto, and T. G. Halsall, *Chem. and Ind.*, 1964, 1751.

as they both derive from *Meliaceous* trees, their constitutions lend weight to the proposed biogenesis of swietenine.

Experimental

Melting points were taken on a Kofler hot-stage apparatus. Specific rotations refer to chloroform solutions except where otherwise specified. Infrared solution spectra were recorded by Mrs. F. Lawrie, Glasgow, on a Unicam S.P. 100 Mark II Spectrophotometer with a prism grating monochromator operated with evacuated optics. Nuclear magnetic resonance spectra were obtained on the Varian Associates A-60 and HR-100 and the Perkin-Elmer R 10 spectrometers, using approximately 0·3M-solutions in deuteriochloroform with tetramethylsilane as internal standard. Rotatory dispersion and circular dichroism measurements[20] were made respectively by Professor W. Klyne, London, and Dr. G. Snatzke, Bonn, to whom we express our thanks. Microanalyses are by Mr. J. M. L. Cameron and his staff, Glasgow. Woelm Grade I alumina, deactivated to the appropriate grade according to Brockmann,[21] was used for chromatography. Chromatoplates both for analytical and preparative use were made by the method of Stahl,[22] using Kieselgel G (Merck).

Extraction of Swietenine and Swietenolide from Swietenia macrophylla *Seeds.*—The seeds used in this investigation were collected in Trinidad during March, through the courtesy of Mr. W. S. Chalmers, Assistant Conservator of Forests, Port of Spain, whose help we acknowledge with pleasure. The milled seeds (8 kg.) were defatted by extraction with light petroleum (b. p. 40—60°) in a Soxhlet apparatus. The dried meal (3·7 kg.) was extracted with chloroform and the concentrated extract diluted with two volumes of light petroleum. The resulting yellow gum was dissolved in ethanol and left overnight. Crude swietenine which separated, m. p. 190—240° (42 gm.), gave, after one crystallisation from chloroform–light petroleum, material (21 g.) of m. p. 250—260°, $[\alpha]_D$ −182° (*c* 2·11). Addition of saturated barium hydroxide solution to the ethanolic mother-liquors precipitated further gummy material. Acidification of the supernatant liquid with dilute hydrochloric acid gave crude swietenolide (30 g.) as a yellow amorphous powder. A portion (2 g.) crystallised from ethyl acetate afforded swietenolide (450 mg.), m. p. 215—222°, $[\alpha]_D$ −125°.

To obtain pure swietenine, the material, m. p. 250—260°, was chromatographed over acid alumina (activity IV) in chloroform–benzene (1 : 9). Elution with this solvent until fractions containing a single component on thin-layer chromatography (t.l.c.) were obtained, followed by elution with chloroform–benzene (1 : 4) afforded pure swietenine, rods from chloroform–light petroleum, m. p. 272—276°, rotatory dispersion ($CHCl_3$): $[\phi]_{600}$ −886, $[\phi]_{589}$ −948, $[\phi]_{312\cdot5}$ −12,810, $[\phi]_{275}$ +364°; $\nu_{max.}$ ($CHCl_3$) 1730 (methyl ester and δ-lactone), 1705 (cyclohexanone), 1650 (ethylenic double bond), 3610, 3546 cm.$^{-1}$ (bonded and unbonded OH) [Found: C, 67·45; H, 7·0. Calc. for $C_{32}H_{40}O_9$: C, 67·6; H, 7·1%].

Hydrogenation of Swietenine.—(*a*) Swietenine (2 g.) in AnalaR acetic acid (200 ml.) was hydrogenated over 10% palladium–charcoal (2 g., Baker) for 12 hr. (hydrogen uptake 385 ml., 3·8 mol.). Working up in the usual manner gave 1680 mg. acid and 310 mg. neutral fractions. The acid fraction crystallised from ether–light petroleum to afford the *octahydro-acid* (VII) (650 mg.), m. p. 153—154°, rotatory dispersion (MeOH): $[\phi]_{589}$ −1700, $[\phi]_{310}$ −9650, $[\phi]_{277\cdot5}$ −875°; p*K* 5·2; $\nu_{max.}$ (Nujol) 1730 cm.$^{-1}$, $\lambda_{max.}$ 202 mμ (ε 6300) (Found: C, 64·65; H, 8·4. $C_{32}H_{48}O_9 \cdot H_2O$ requires C, 64·6; H, 8·45%). The residue obtained from the mother-liquors of crystallisation of the octahydro-acid (1·0 g.) was methylated with diazomethane in ether. Chromatography of the product over acid alumina (activity III) with benzene–ether mixtures afforded the *methyl ester* (VIIa) (880 mg.), m. p. (from ether–light petroleum) 164—165°, $[\alpha]_D$ −179° (*c* 1·22), $\lambda_{max.}$ 204 mμ (ε 5670); $\nu_{max.}$ (CCl_4) 1735 (methyl ester and cyclohexanone), 3609, 3527 cm.$^{-1}$ (unbonded and bonded OH) (Found: C, 66·6; H, 8·4. $C_{33}H_{50}O_9$ requires C, 67·1; H, 8·55%). Methylation of pure octahydro-acid produced material indistinguishable from the ester obtained from mother-liquors as above. Oximation of the octahydro-acid with an excess of hydroxylamine hydrochloride in ethanol–pyridine under reflux afforded the *octahydro-acid oxime*, (VIIb) needles from chlorform–benzene, m. p. 251—254° (Found: C, 63·2; H, 7·85. $C_{32}H_{51}NO_{10}$ requires C, 63·05; H, 8·45%). The octahydro-acid methyl ester was recovered unchanged after storage with osmium tetroxide (1 mol.) in ether–dioxan (1 : 1) for 72 hr. at 20°.

[20] G. Snatzke, *Tetrahedron*, 1965, **21**, 421.
[21] H. Brockman and H. Schodder, *Ber.*, 1941, **74**, 73.
[22] E. Stahl, *Chem.-Ztg.*, 1958, **82**, 323.

(*b*) Swietenine (620 mg.) in AnalaR ethyl acetate (75 ml.) was hydrogenated for 24 hr. over platinum oxide (1 g.), when hydrogen absorption had ceased. The neutral product (294 mg.) gave *dihydroswietenine*, (VIIc) (98 mg.), rods from ethyl acetate, m. p. 224—229°, $\nu_{max.}$ (CCl_4) 1738, shoulders 1730sh, and 1750sh (δ-lactone, methyl and dihydrotiglate esters, cyclohexanone), 3606, 3525 cm.$^{-1}$ (unbonded and bonded OH), n.m.r. bands at τ 2·56, 2·45, and 3·63 (α- and β-furanic protons), τ 4·32 (C-17 proton), disappearance of tiglate signals at τ 5·3 and τ 8·2—8·3 (Found: C, 67·1; H, 7·5. $C_{32}H_{42}O_9$ requires C, 67·35; H, 7·4%).

Alkaline Hydrolysis of Swietenine.—The following conditions chosen from a number of trial experiments represent those giving the best yields of demethyldetigloylisoswietenine. Swietenine (1 g.), dissolved in ethanolic potassium hydroxide solution (5%; 100 ml.), was kept at 100° for 10 min. under nitrogen. Acidification of the cooled solution with 6N-hydrochloric acid, dilution with water, and extraction into ethyl acetate gave, on separation in the usual way, an acid fraction (850 mg.) which crystallised from chloroform, to furnish *demethyldetigloylisoswietenine* (VIII), (250 mg.), rods from acetone–ether, m. p. 249—251°, $[\alpha]_D$ −75° (*c* 1·69 in $COMe_2$), p*K* 4·85 (Found: C, 64·2; H, 6·65. $C_{26}H_{32}O_8 \cdot H_2O$ requires C, 63·65; H, 7·0%). Methylation of this acid with diazomethane afforded *detigloylisoswietenine* (IX), needles from chloroform–ether, m. p. 243—246°, rotatory dispersion (*c* 1·10 in MeOH) $[\phi]_{500}$ −170, $[\phi]_{307}$ −3165, $[\phi]_{271}$ +1545, $[\phi]_{255}$ +937°; Circular dichroism (*c* 2·34 in dioxan) *: 326(0), 309i(−0·85), 297(−1·24), 292i(−1·16), 260(0); $[\alpha]_D$ −67°; $\nu_{max.}$ ($CHCl_3$) 1730 (methyl ester, δ-lactone, and cyclohexanone), 3604, 3530 cm.$^{-1}$ (unbonded and bonded OH) (Found: C, 66·75; H, 6·9. $C_{27}H_{34}O_8$ requires C, 66·65; H, 7·05%). Further quantities of detigloylisoswietenine were obtained by methylation of the residue from the chloroformic mother-liquors, followed by chromatography over acid alumina, and also from the neutral product of the hydrolysis. In one experiment the acidified solution from the hydrolysis was diluted with water and distilled to separate volatile acids. Saturation of the distillate with ammonium sulphate and extraction into ether furnished in this way 17 mg. crude crystalline acid (from 100 mg. swietenine), the *p*-bromophenacyl ester of which, m. p. 67—68°, did not depress the m. p. of *p*-bromophenacyl tiglate.

Isoswietenine (X).—Detigloylisoswietenine (56 mg.) and redistilled tigloyl chloride (1 ml.; b. p. 45—50°/17 mm.) were kept in AnalaR pyridine at 0° for 12 hr. Working up gave a black tar which, on chromatography over acid alumina (Grade IV) and elution with chloroform–benzene (1 : 9), afforded *isoswietenine* (45 mg.), m. p. (from ethyl acetate–light petroleum) 213—215°, rotatory dispersion (MeOH): $[\phi]_{589}$ −1130, $[\phi]_{300}$ −2100, $[\phi]_{290}$ −850°; $\nu_{max.}$ (Nujol) 1705 (tiglate ester), 1725 (methyl ester, δ-lactone, and cyclohexanone), 3100, 1500, 879 (furan), 3500 (OH) cm.$^{-1}$ (Found: C, 67·2; H, 7·1. $C_{32}H_{40}O_9$ requires C, 67·6; H, 7·1%).

Detigloylswietenine (XI).—Swietenine (200 mg.) and osmium tetroxide (90 mg., 1 mol.) were kept in tetrahydrofuran (3 ml.) and pyridine (3 ml.) in the dark for 16 hr. Aqueous sodium hydrogen sulphite solution (10 ml.; 5%) was added and the mixture stirred for ½ hr. The crude product, obtained by chloroform extraction, was dissolved in methanol (5 ml.) and treated with an excess of aqueous sodium periodate solution for 16 hr. The crude pyruvate ester obtained by dilution with water and extraction into chloroform was hydrolysed with aqueous sodium hydrogen carbonate solution at 20° for 15 min. *Detigloylswietenine* (IV) (100 mg.) was obtained from the reaction product by preparative t.l.c., and crystallised from chloroform–ether–light petroleum, m. p. 200—204° $[\alpha]_D$ −62°; rotatory dispersion (*c* 1·08 in MeOH); $[\phi]_{500}$ −670, $[\phi]_{309}$ −6830, $[\phi]_{274}$ +95, $[\phi]_{234}$ −9575°; circular dichroism (*c* 1·28 in dioxan); 325(0), 308i(−1·23), 297(−1·96), 292·5i(−1·86), 258(0) (Found: C, 65·7; H, 6·85. $C_{27}H_{34}O_8, 1/2H_2O$ requires C, 65·45; H, 7·1%). Isomerisation under the conditions used for dehydrodetigloylswietenine (see p. 6947) afforded detigloylisoswietenine in almost quantitative yield.

p-*Iodobenzoate* (II) *of Detigloylswietenine.*—Detigloylswietenine (30 mg.) was treated with *p*-iodobenzoyl chloride (20 mg.) in pyridine (2 ml.) for 16 hr. Chromatography over acid alumina (Grade IV) in benzene afforded *detigloylswietenine* p-*iodobenzoate* (II), rods from chloroform–ether–light petroleum, m. p. 271—273° (Found: C, 56·3; H, 5·6. $C_{34}H_{37}IO_9$ requires C, 57·0; H, 5·2%).

Trioxo-ester (XII).—Detigloylisoswietenine (IX) (34 mg.) was oxidised by the Sarrett procedure. The product (31 mg.), obtained in the usual manner, showed three components on t.l.c. Chromatography over acid alumina (Grade IV) furnished on elution with chloroform–benzene (1 : 19) the *trioxo-ester* (XII) (15 mg.), m. p. (from chloroform–ether) 231—234°, $[\alpha]_D$

* For notation see ref. 20.

−288° rotatory dispersion ($CHCl_3$): $[\phi]_{589}$ −1100, $[\phi]_{322\cdot5}$ −12,200, $[\phi]_{270}$ +4860°, $\nu_{max.}$ ($CHCl_3$) 1730, 1745sh cm.$^{-1}$ (ketonic carbonyls, methyl ester, and δ-lactone) (Found: C, 67·0; H, 6·35. $C_{27}H_{30}O_8$ requires C, 67·2; H, 6·25%). Detigloylswietenine (IV) (15 mg.) treated under the same conditions afforded the same trioxo-ester (m. p. mixed m. p. and t.l.c.). as also did oxidation of dehydrodetigloylisoswietenine (XIII) with the Jones reagent (see below).

Dehydroswietenine (V).—(*a*) Swietenine (200 mg.) and chromium trioxide (100 mg.) were left in dry pyridine at 20° for 16 hr. The crude semi-crystalline product (190 mg.) obtained by addition of an excess of methanol, removal of solvents *in vacuo*, dilution with water, and extraction into chloroform gave, on chromatography over acid alumina (Grade IV), *dehydroswietenine* (V) (119 mg.), rods from chloroform–ether, m. p. 261—265°, rotatory dispersion ($CHCl_3$): $[\phi]_{589}$ −925, $[\phi]_{400}$ −3300, $[\phi]_{375}$ −2800, $[\phi]_{350}$ −3350, $[\phi]_{312\cdot5}$ −7900, $[\phi]_{282\cdot5}$ −2720°, $\nu_{max.}$ ($CHCl_3$) 1730 (methyl ester and δ-lactone), 1705 (ketones), and 1650 cm.$^{-1}$ (olefinic double bond) (Found: C, 67·45; H, 6·6. $C_{32}H_{38}O_9$ requires C, 67·8; H, 6·75%).

(*b*) Dehydroswietenine was obtained more simply and in improved yield by oxidation with the Jones reagent. Swietenine (1 g.) in AnalaR acetone (40 ml.) and an excess of 7·5N-chromic acid was kept at 0° for 16 hr. Working-up in the usual way gave a gum (980 mg.) which crystallised from chloroform–ether to give dehydroswietenine (638 mg.), m. p. 261—264°.

Dehydroswietenine changed spontaneously on storage in air and light at 20°. Thus, a specimen of m. p. 259—263° had, after three weeks, m. p. 115—140° and showed by t.l.c. one more-polar component in addition to unchanged dehydroswietenine.

Reduction of Dehydroswietenine to Swietenine.—(*a*) Dehydroswietenine (22 mg.) and AnalaR zinc dust (220 mg.) were refluxed in AnalaR acetic acid (2 ml.) for 10 min. Removal of zinc and solvent and filtration of the residue in chloroform through acid alumina (Grade IV) afforded swietenine (16 mg.), m. p. (from chloroform–light petroleum) 271—274° alone and on admixture with swietenine and indistinguishable from it in its i.r. spectrum and t.l.c. behaviour.

(*b*) Dehydroswietenine (17 mg.) was kept with an excess of sodium borohydride in methanol at 20° for 1 hr. The product, obtained by dilution with water, acidification with aqueous acid, and extraction into ethyl acetate, afforded on chromatography over acid alumina (Grade IV) and crystallisation a product (5 mg.) identical in m. p., mixed m. p., t.l.c., and i.r. spectrum with swietenine.

Dehydrodetigloylisoswietenine (XIV).—Dehydroswietenine (V) (240 mg.) dissolved in 2·5% potassium hydroxide in dioxan–methanol (1 : 1; 0·8 ml.) was kept at 20° for 0·5 hr. and then acidified with 6N-hydrochloric acid and diluted with water until crystallisation commenced. Recrystallisation from chloroform–ether afforded dehydrodemethylswietenine (180 mg.), m. p. 272—276°. Methylation with diazomethane regenerated dehydroswietenine (m. p., mixed m. p., i.r. spectrum). Swietenine was recovered unchanged under these hydrolytic conditions.

Dehydroswietenine (V) (1 g.) was refluxed in 2·5% potassium hydroxide in ethanol (100 ml.) in an atmosphere of nitrogen for 10 min. The solution was acidified and diluted with water as before, affording a crystalline solid (594 mg.), m. p. 258—265°. Extraction of the aqueous-ethanolic mother liquors with ethyl acetate afforded a second crop (250 mg.), m. p. 243—257°; methylation gave a mixture of four products (t.l.c.) which were not further investigated. Two crystallisations from acetone–ether–light petroleum of the material, m. p. 258—265°, gave rods of *dehydrodemethyldetigloylisoswietenine*, m. p. 264—267°, $[\alpha]_D$ −61° (*c* 1·32 in Me_2CO) (Found: C, 65·9; H, 6·65. $C_{26}H_{30}O_8$ requires C, 66·36; H, 6·45%). Methylation of a methanolic solution with ethereal diazomethane afforded *dehydrodetigloylisoswietenine* (XIV), rods from chloroform–ether, m. p. 242—246°, $[\alpha]_D$ −74° (*c* 1·21); $\nu_{max.}$ ($CHCl_3$) 1730 (methyl ester, δ-lactone, ketones) and 3612 cm.$^{-1}$ (unbonded OH) (Found: C, 67·05; H, 6·65. $C_{27}H_{32}O_8$ requires C, 66·9; H, 6·65%).

Dehydrodetigloylisoswietenine changed spontaneously on exposure to light and air in the same way as dehydroswietenine (drop in m. p. and yellow coloration).

Reduction of Dehydrodemethyldetigloylisoswietenine.—Dehydrodemethyldetigloylisoswietenine (680 mg.) was refluxed with AnalaR zinc dust (7·4 g.) in AnalaR acetic acid (150 ml.) for 2 hr. Removal of the excess of zinc and acetic acid left a gum (670 mg.) which crystallised from chloroform. Methylation afforded two products (t.l.c.) which were separated by chromatography over acid alumina (Grade IV). Chloroform–benzene (3 : 7) eluted the non-crystalline 3-acetoxydetigloylisoswietenine (69 mg.) [n.m.r. spectrum very similar to that of detigloylisoswietenine, except for the additional signals at τ 5·41 (C*H*·OAc) and τ 7·93 (O·CO·CH_3) and separation of

the methyl signal (9H) in detigloylisoswietenine at τ 9·0 into three separate bands at τ 8·89, 9·00, 9·08]. Chloroform eluted detigloylisoswietenine (IX) (430 mg.), identical (m. p., mixed m. p., n.m.r. spectrum) with the compound prepared by alkaline hydrolysis and methylation of swietenine.

Oxidation of Dehydrodetigloylisoswietenine (XIV).—Oxidation of dehydrodetigloylisoswietenine (20 mg.) with the Sarrett reagent furnished, on addition of ether to the gummy reaction product, crystalline material, which was filtered through acid alumina (Grade IV) in chloroform–benzene (1 : 19), and then afforded the trioxo-ester (XII) (15 mg.), identical (m. p., mixed m. p., t.l.c.) with the substance previously obtained from detigloylisoswietenine. Oxidation with the Jones reagent gave similar results.

Dehydrodetigloylswietenine (XIII).—Dehydroswietenine (V) (250 mg.) and osmium tetroxide (125 mg.) were kept in tetrahydrofuran (10 ml.) and pyridine (10 ml.) in the dark for 16 hr. Decomposition with aqueous sodium hydrogen sulphite and extraction into chloroform gave a mixture of epimeric diols (150 mg.) and unchanged dehydroswietenine (70 mg.), which were separated by preparative t.l.c. The diol mixture (150 mg.) in methanol (10 ml.) was oxidised by adding sodium periodate (100 mg.) in water (2 ml.), and storing the mixture for 16 hr. at 20°. Addition of saturated sodium hydrogen carbonate solution to hydrolyse the pyruvate ester and extraction after 1 hr. into chloroform furnished *dehydrodetigloylswietenine* (XIII) (140 mg.), m. p. (from chloroform–ether) 210—214°, $[\alpha]_D$ −54° (Found: C, 64·35; H, 6·85. $C_{27}H_{32}O_8,H_2O$ requires C, 64·55; H, 6·80%).

Isomerisation of Dehydrodetigloylswietenine (XIII) *to Dehydrodetigloylisoswietenine* (XIV).—Dehydrodetigloylswietenine (30 mg.) was heated with ethanolic potassium hydroxide (2·5%) at 100° for 10 min. The product obtained in the usual way was methylated with diazomethane and when crystallised from chloroform–ether–light petroleum afforded dehydrodetigloylisoswietenine [(XIV), 20 mg.], m. p. and mixed m. p. 240—245° (i.r. and t.l.c. comparison). The mother-liquors from the crystallisation contained (t.l.c.) as main constituent a compound similar in polarity to dehydrodetigloylswietenine, which, however, oxidised to a substance more polar than the trione (XII) and may be the 5-epimer of dehydrodetigloylisoswietenine.

Reduction of Dehydrodetigloylswietenine (XIII) *to Detigloylswietenine* (IV).—Dehydrodetigloylswietenine (10 mg.), reduced with sodium borohydride (10 mg.) in methanol (2 ml.) at 0° afforded, after purification by preparative t.l.c., detigloylswietenine (7 mg.) identical in m. p., mixed m. p., i.r. spectrum, and t.l.c. with material prepared direct from swietenine by the Kupchan procedure.

Oxidation of Dehydrodetigloylswietenine (XIII).—Dehydrodetigloylswietenine (15 mg.) on oxidation with the Jones reagent afforded, in almost quantitative yield, the trioxo-ester (XII)(m. p., mixed m. p. i.r. spectrum, n.m.r., and t.l.c.), previously obtained from oxidation of both detigloylisoswietenine and dehydrodetigloylisoswietenine.

Nor-aldehyde (VI).—(*a*) Demethyldetigloylisoswietenine (120 mg.) and lead dioxide (B.D.H., 90 mg.) were refluxed in AnalaR acetic acid (5 ml.) for 3 hr. The neutral product (106 mg.), obtained in the usual way, consisted of two components (t.l.c.) which were separated by chromatography over acid alumina (Grade IV). Benzene eluted the *nor-aldehyde acetate* (VIa) (28 mg.), needles from chloroform–ether, m. p. 274—279°, $[\alpha]_D$ −34° (*c* 0·9) (Found: C, 69·45; H, 7·1. $C_{27}H_{32}O_7$ requires C, 69·2; H, 6·9%). Benzene–chloroform mixtures eluted the *nor-aldehyde* (VI), rods from chloroform–benzene–light petroleum, m. p. 234—237°, $[\alpha]_D$ −47° (*c* 1·2), $\nu_{max.}$ (CCl_4) 1752 (δ-lactone), 1734 (aldehyde), 1721 (cyclohexanone), 3632 $cm.^{-1}$ (free OH) (Found: C, 70·35; H, 7·2. $C_{25}H_{30}O_6$ requires C, 70·4; H, 7·1%).

(*b*) Demethyldetigloylisoswietenine (290 mg.) and lead tetra-acetate (400 mg.) were kept in AnalaR acetic acid (20 ml.) in the dark at 20° for 3 days. Addition of water and extraction with chloroform gave a neutral fraction (260 mg.) which crystallised from chloroform–light petroleum to afford the nor-aldehyde (225 mg.), identical (m. p., mixed m. p., t.l.c, n.m.r. spectrum) with material obtained as described in (*a*). Acetylation with acetic anhydride–pyridine at 20° gave the acetate obtained as described in (*a*).

Reaction of the Nor-aldehyde (VI) *with Hydrogen Chloride in Methanol.*—The nor-aldehyde (90 mg.) was heated on a steam-bath in dry 0·1N-methanolic hydrogen chloride (1·5 ml.) for 20 min. Working-up with sodium carbonate, removal of solvent and elution of the product from neutral alumina (V) with benzene gave a homogeneous material (t.l.c.) (53 mg.) which, however, did not crystallise. Acetylaction with acetic anhydride–pyridine at room temperature and filtration of the product through acid alumina (Grade IV) afforded the *methyl ether methyl*

ester acetate (VIb (35 mg.), needles from chloroform–ether, m. p. 184—186°, $\nu_{max.}$ (Nujol) 1740 (methyl ester and aldehyde), 1710 cm.$^{-1}$ (cyclohexanone), n.m.r. signals at τ 6·67 (3H, singlet, OCH_3) and τ 6·26 (3H, singlet, CO_2CH_3), disappearance of the C-17 proton at τ 4·60 in the nor-aldehyde (Found: C, 67·9; H, 7·6. $C_{29}H_{38}O_8$ requires C, 67·7; H, 7·45%). The same compound was obtained by exposure of the nor-aldehyde acetate to the same acidic conditions.

Oxidation of the Nor-aldehyde to the Dioxo-aldehyde (XV).—The nor-aldehyde (85 mg.) was oxidised with the Jones reagent at 0° in the usual way. Chromatography of the gummy product (70 mg.) over acid alumina (Grade IV) in benzene afforded the *dioxo-aldehyde* (XV) (44 mg.), needles from chloroform–ether–light petroleum, m. p. 218—221°, $[\alpha]_D$ −193° (*c* 1·36); $\nu_{max.}$ (CCl_4) 1751 (aldehyde and δ-lactone) and 1722 cm.$^{-1}$ (cyclohexanones) (Found: C, 70·15; H, 6·75. $C_{25}H_{28}O_6$ requires C, 70·75; H, 6·65%). The same substance was also obtained by oxidation of the nor-aldehyde with the Sarrett reagent.

Formation of the γ-Lactone (XVI).—The nor-aldehyde (VI) (116 mg.) dissolved in ethanol (7 ml.) and 0·5N-aqueous sodium hydroxide (7 ml.) was refluxed for 1 hr. in an atmosphere of nitrogen. Acidification with 6N-hydrochloric acid and extraction into ethyl acetate afforded a gummy mixture of two substances (t.l.c.). They were separated by preparative t.l.c. using methanol–chloroform (1 : 50) for development and a water spray for detection. Extraction of the more polar band with ethyl acetate furnished the *γ-lactone* (XVI) (70 mg.), rods from chloroform–light petroleum, m. p. 242—246°, $[\alpha]_D$ +111° (*c* 1·02), $\nu_{max.}$ ($CHCl_3$) 1770 (γ-lactone), 1732 (δ-lactone), 3620, 3587 cm.$^{-1}$ (unbonded and bonded OH) (Found: C, 67·85; H, 7·5. $C_{25}H_{30}O_6,H_2O$ requires C, 67·55; H, 7·25%).

The second component (40 mg.) recovered from the plate, although homogeneous, did not crystallise, nor did its acetate, and these were not further investigated. Acetylation of the γ-lactone with acetic anhydride–pyridine at 20° furnished in nearly quantitative yield the *γ-lactone acetate* (XVIa), rods from chloroform–ether, m. p. 274—278°, $\nu_{max.}$ (Nujol) 1770 (γ-lactone), 1730 cm.$^{-1}$ (δ-lactone and acetate) (Found: C, 68·8; H, 6·85. $C_{27}H_{32}O_7$ requires C, 69·2; H, 6·9%).

Oxidation of the γ-Lactone (XVI) *to the Dehydro-γ-lactone* (XVII).—The γ-lactone (180 mg.) in AnalaR acetone (5 ml.) was oxidised with an excess of 7·5N-chromic acid at 0°. Work-up as usual afforded the *dehydro-γ-lactone* (XVII) (120 mg.), needles from chloroform–ether, m. p. 248—251°, $[\alpha]_D$ +190° (*c* 0·92 in pyridine), $\nu_{max.}$ ($CHCl_3$) 1781 (γ-lactone), 1762 (bicyclo[3,2,1]-octanone carbonyl), 1735 cm.$^{-1}$ (δ-lactone) (Found: C, 70·15; H, 6·35. $C_{25}H_{28}O_6$ requires C, 70·75; H, 6·65%).

Reduction of the Dehydro-γ-lactone (XVI).—The dehydro-γ-lactone (29 mg.) was kept with sodium borohydride (15 mg.) in methanol (10 ml.) for 1·5 hr. Acidification and extraction into chloroform gave a gum consisting of two components which were separated by preparative t.l.c. Recovery of the more polar band furnished the γ-lactone (25 mg.), m. p. 240—245°, alone and mixed with authentic γ-lactone. Recovery of the other band gave the 1-epi-γ-lactone (3 mg.), which did not crystallise, $\nu_{max.}$ ($CHCl_3$) 1758 (H-bonded γ-lactone), 1748sh (δ-lactone), 3621 (unbonded OH), 3550, 3350vbr cm.$^{-1}$ (bonded OH).

Reaction of the Dehydro-γ-lactone with Alkali.—The dehydro-γ-lactone (52 mg.) was heated in ethanol (3·5 ml.) and 0·5N-aqueous sodium hydroxide (3·5 ml.) on a steam-bath in a nitrogen stream for 1 hr. The acidic fraction (34 mg.) in methanol was methylated with ethereal diazomethane. Filtration in chloroform through acid alumina (Grade IV) afforded the *hydroxy-ester* (XVIIIa) (25 mg.), rods from chloroform–light petroleum, m. p. 209—212°, $[\alpha]_D$ +120° (*c* 1·1), $\nu_{max.}$ ($CHCl_3$) 1750 (bicyclo[3,2,1]octanone carbonyl), 1731 (δ-lactone), 3614 cm.$^{-1}$ (unbonded OH) (Found: C, 68·3; H, 7·1. $C_{26}H_{32}O_7$ requires C, 68·4; H, 7·1%).

Crystallisation of the neutral fraction from chloroform–light petroleum afforded the dehydro-γ-lactone (15 mg.) (m. p., mixed m. p., t.l.c., and i.r. spectrum).

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