Lichens and Fungi. Part XII.[1] Dehydration and Isomerization of Stictane Triterpenoids

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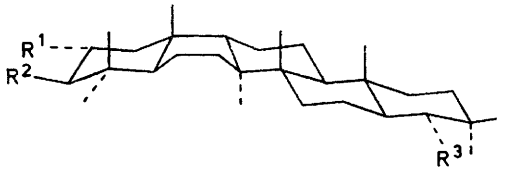
N.m.r. spectral data of a number of stictane derivatives have provided further support for the structure proposed for stictane, and the absence of an 8β-methyl group in this series of compounds has been verified.

In Part XI [1] we reported the isolation from lichens of the *Sticta* genus and some chemical transformations of ten triterpenoids derived from a new parent triterpenoid to which we gave the name stictane. We now report dehydration, isomerization, and spectroscopic studies which confirm that stictane (1a) and the related flavicane (2a) have an 8α-methyl group and a boat structure for ring B rather than the usual 8β-methyl group and chair ring B, hitherto found in pentacyclic triterpenoids.

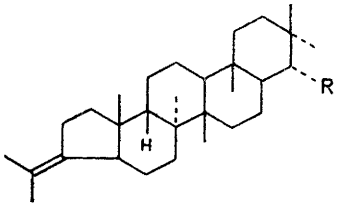
Attention has been drawn [1] to the close similarity

[1] Part XI, W. J. Chin. R. E. Corbett, C. K. Heng, and A. L. Wilkins, *J.C.S. Perkin I*, 1973, 1437.

between the mass spectra of stictane and flavicane and those of the pentacyclic triterpenoids hopane, 18α-oleanane, 14α-taraxerane, and gammacerane. In all these spectra the base peak is at *m/e* 191 and is attributed to two fragments each of the same mass resulting from initial cleavage of the 8,14-bond.[2] The production of these two fragments requires that these pentacyclic structures should contain four ring A/B methyl groups and four ring D/E methyl groups. Furthermore, the presence of oxygen functions attached to the terminal rings at C-3 in ring A and C-22 in ring E, in the ten stictanes so far isolated,[1] implies, on biogenetic grounds, that cyclization is initiated in the usual manner by protonation of squalene 2,3-oxide and terminated without proton, methyl, or backbone rearrangements, by hydration of a ring E cation with loss of a proton.[1] These mass spectral and biogenetic observations imply that methyl groups are to be expected at C-4(2), C-10, C-8, C-14, and C-18, and two in ring E, and the stictane structure fulfils this requirement.



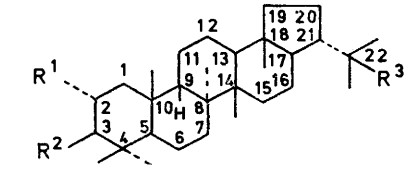
	R^1	R^2	R^3
(1) a;	H	H	H
b;	H	OH	OAc
c;	H	H	OAc
d;	H	H	OH
e;	OAc	OAc	OH



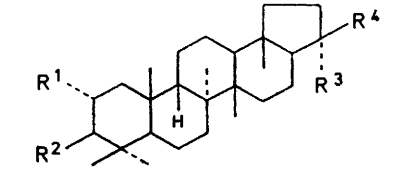
(3) a; R = OAc
b; R = OH

Deydration of 22α-acetoxystictan-3β-ol (1b) with phosphorous pentachloride gave the 5(4 ⟶ 3)*abeo*-acetate (3a).[1] A comparison of the methyl resonances of this acetate with those of 22α-acetoxystictane (1c) reveals that significant changes have occurred in the C-8, C-14, C-18, and one of the C-21 methyl signals (Table 1). Similar changes distinguish the n.m.r. spectra of the 5(4 ⟶ 3)*abeo*-alcohol (3b) and stictan-22α-ol (1d), and indicate that a conformational transmission effect[3] is present in 5(4 ⟶ 3)*abeo*-stict-3-ene derivatives. Such an effect is not present in 5(4 ⟶ 3)*abeo*-triterpenes having the usual *trans,anti,trans*-ABC ring structure with rings B and C in the usual rigid chair conformation, as for example in hopane and lupane, *etc.* (Table 2). The greater flexibility of the boat ring B will account for the transmission effect observed in the *abeo*-stictanes.

In 5(4 ⟶ 3)*abeo*-stict-3-ene derivatives the C-8 methyl resonance is *ca.* 0.08 p.p.m. downfield from the C-8 methyl resonance in corresponding stictane derivatives. The C-8 methyl group must be deshielded by the exocyclic isopropylidene group. In the other 5(4 ⟶ 3)-*abeo*-triterpenes listed in Table 2, all of which have 8β-methyl groups, this methyl group is neither shielded nor deshielded. Molecular models indicate that a C-8 methyl group, α-oriented in a boat ring B structure, would be suitably positioned for that methyl group to be deshielded as in 5(4 ⟶ 3)*abeo*-stict-3-ene derivatives.



	R^1	R^2	R^3
(2) a;	H	H	H
b;	H	OAc	H
c;	H	OH	H
d;	OAc	OAc	H
e;	H	H	$O_2C\cdot CCl_3$



	R^1	R^2	R^3	R^4
(4) a;	OAc	OAc	$C(:CH_2)Me$	H
b;	H	OAc	$C(:CH_2)Me$	H
(5)	OAc	OAc	$:CMe_2$	

Dehydration of 2α,3β-diacetoxystictan-22α-ol (1e)[1] with phosphorus pentachloride gave a mixture (4 : 1) of the isomeric diacetates (4a) and (5). A comparison of the spectral data of (5) with those of (2d) and of flavica-2,21-diene (7a)[1] with those of (7b)[1] (Table 1) revealed the absence of conformational transmission effects in these ring-E-contracted stictanes, the flavic-21-enes, in direct contrast to the ring-A-contracted stictanes. There is a similar absence of a conformational transmission effect in hop-21-ene[4] (8). The C-18 methyl group in all

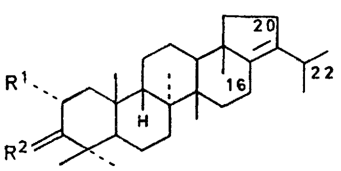
[2] M. N. Galbraith, C. J. Miller, J. W. L. Rawson, E. Ritchie, J. S. Shannon, and W. C. Taylor, *Austral. J. Chem.*, 1965, **18**, 226.

[3] D. H. R. Barton, A. J. Head, and P. J. May, *J. Chem. Soc.*, 1957, 935.

[4] R. E. Corbett and R. A. J. Smith, *J. Chem. Soc.* (*C*), 1967, 1622.

these 21-enes is very strongly shielded and its signal appears at or near δ 0.57 (Table 1).

Each of the diacetates (4a) and (5) was isomerised with formic acid in chloroform into the diacetate (6a) Compound (5) also gave (6a) with trichloroacetic acid in chloroform, but (4a) gave 2α,3β-diacetoxy-22-trichloroacetoxyflavicane (2e) with this reagent. The acetate



	R^1	R^2
(6) a;	OAc	α-H,OAc
b;	H	α-H,OAc
c;	H	α-H,OH
d;	OH	α-H,OH
e;	OAc	α-H,OH
f;	OH	α-H,OAc
g;	OAc	O
h;	H	O

(6a) $\xrightarrow{(i)}$ (6d) $\xrightarrow{(ii)}$ (6e) + (6f) (separate)

(6e) $\xrightarrow{(iii)}$ (6g) $\xrightarrow{(iv)}$ (6h) $\xrightarrow{(v)}$ (6c) $\xrightarrow{(vi)}$ (6b)

SCHEME Reagents: i, KOH–EtOH; ii, Ac_2O–pyridine; iii, Jones oxidation; iv, Ca–liq. NH_3; v, $LiAlH_4$; vi, Ac_2O–pyridine

(6b) and the alcohol (6c) were prepared as outlined in the Scheme. The similarity of the three ring E methyl resonance (Table 3) and of the multiplets arising from the five protons allylic to the 17,21-double bond (Figure 1) in the n.m.r. spectra of compounds (9a and b) and (6a—c) is to be expected. The structure proposed for flavicane (2a) [1] in which rings CDE are antipodally related to rings CDE of 21α*H*-hopane about the BC ring junction implies this spectral identity. The splittings of $16\text{-}H_2$, $20\text{-}H_2$, and 22-H (Figure 1) by the adjacent protons at C-15, C-19, C-29, and C-30 must be the same in all the compounds. Also since rings D and E of both the hopenes and the flavicenes are stereochemically similar the chemical shifts of the lines of all the patterns must be the same. Any difference in the stereochemistry of rings CDE of flavicane, a boat ring C or a *cis*-CD-ring junction for example, would result in a change in the absolute values of the chemical shifts because of a change in the anisotropy, and in the splitting patterns because of a change in the flexibility of ring D.

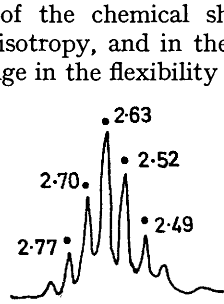


FIGURE 1 Multiplet typical of allylic protons at C-16 (2 H), —20 (2 H), and —22 (1 H) in compounds (9a and b) and (6a—c)

While a 17,21-double bond has no appreciable effect on the signals of the C-8 and C-10 methyl groups in the

TABLE 1

Chemical shifts (δ) of methyl groups

Compound	4β	4α	10β	8α	14β	18β	21α	21β
22α-Acetoxy-5(4 ⟶ 3)*abeo*-stict-3-ene (3a)	1.56,	1.72	0.75	1.07	0.96	0.85	0.89	0.93
22α-Acetoxystictane (1c)	0.82	0.85	0.89	1.14	0.92	0.82	0.85	0.92
5(4 ⟶ 3)*abeo*-Stict-3-en-22α-ol (3d)	1.56,	1.72	0.76	1.06	0.97	0.76	0.89	0.98
Stictan-22α-ol (1d)	0.81	0.86	0.90	1.14	0.91	0.73	0.86	0.98
							22	
2α,3β-Diacetoxyflavic-21-ene (5)	0.89	1.04	0.89	1.16	0.89	0.56	1.56,	1.72
2α,3β-Diacetoxyflavicane (2d)	0.90	1.03	0.90	1.16	0.90	0.65	0.79,*	0.89 *
Flavica-2,21-diene (7a)	0.92	0.89	0.89	1.12	0.89	0.58	1.56,	1.72
Flavic-2-ene (7b)	0.92	0.89	0.89	1.13	0.89	0.65	0.79,*	0.90 *
	4β	4α	10β	8β	14α	18α	22	
Hop-21-ene * (8)	0.78	0.81	0.83	0.95	0.94	0.56	1.56	1.72
21α*H*-Hopane *	0.78	0.81	0.83	0.95	0.92	0.64	0.77 †	0.87 †

* Ref. 8. † *J* 6—7 Hz.

TABLE 2

Substituent effects (p.p.m.)

Ring A/5(4 ⟶ 3)*abeo*-3-ene	4β	4α	10β	C-8	C-14	Other		
Stictane series	(+0.75,	+0.86)	−0.14	−0.08	+0.05	+0.03	+0.03	0.00
Hopane series [a]	(+0.73,	+0.88)	−0.24	0.00	0.00	0.00	0.00	0.00
Lupane series [b]	(+0.74,	+0.89)	−0.23	+0.01	0.00	0.00	0.00	0.00
Allobetulane series [c]	(+0.76,	+0.88)	−0.22	0.00	0.00			
Dammarane series [d]	(+0.75,	+0.89)	−0.23	0.00	0.00			
Ring E/21-ene						C-18	C-22	
Flavicane series	0.00	0.00	0.00	0.00	0.00	−0.07	(+0.77,	+0.83)
21α*H*-Hopane series	0.00	0.00	0.00	0.00	0.02	−0.08	(+0.79,	+0.84)

* Where more than one example was available the average effect is recorded.

[a] S. Huneck and J. M. Lehn, *Bull. Soc. chim. France*, 1963, 1702. [b] J. M. Lehn and G. Ourrison, *Bull. Soc. chim. France*, 1962, 1137. [c] J. M. Lehn and A. Vystreil, *Tetrahedron*, 1963, **19**, 1733. [d] J. M. Lehn, *Bull. Soc. chim. France*, 1962, 1832.

hopane series it has a pronounced effect on the signals from these methyl groups in the flavicane series. A conformational transmission effect does not appear to operate in the hopane compounds but is clearly seen in the flavicane derivatives (Table 3). On the basis of the proposed flavicane structure the tendency to distortion of ring C caused by the introduction of a further element of strain into rings D and E, the 17 21-double bond, is reduced by some flexing of the relatively mobile boat ring B, and thereby gives rise to the observed changes in the chemical shifts of the C-10, C-8, and C-14 methyl groups. In the hop-17(21)-ene series, the rigidity of the all-chair pentacyclic structure precludes such flexing and the steric strain imposed by the 17,21-double bond is largely absorbed in rings D and E. In the case of flavic-21-ene compounds the presence of the two chair rings, C and D, between ring B and the exocyclic isopropylidene group accounts for the suppression of any transmission of bond angle strain to ring B from ring E.

The ability of lanthanoid derivatives such as tris-(dipivaloylmethanato)europium [Eu(dpm)$_3$] to produce, in the n.m.r. spectra of alcohols, a spectacular increase in dispersion is well established,[5] and attention has been drawn to the use of this shift reagent for determining the number of methyl groups in a triterpenoid and the location of their attachment to the carbon framework.[6] Buckley *et al.*[6] have shown that for the purposes of comparison it is convenient to normalize the results to give a value of 10.0 to the shift of the 4β methyl group in the case of 3β-hydroxy-triterpenoids. Because of the linear relationships established for concentration and temperature the normalization procedure removes the need for precisely defined experimental conditions.[6]

The normalized chemical shifts of methyl groups in flavican-3β-ol (2c) and flavic-17(21)-en-3β-ol (6c) have been measured and compared with those determined for 18α-oleanan-3β-ol (10) and dammara-20,24-diene-3β-ol (11) (Table 4). Clearly in each of compounds (2c), (6c), (10), and (11), the europium atoms must occupy the same mean position relative to the 3β-hydroxy- and 4α-, 4β-, and 10β-methyl groups common to each of these compounds. However the differences apparent in the normalized chemical shifts of the C-8 and C-14 methyl groups of (2c) and (6c), when compared with those of the 8α- and 14β-methyl groups of (10) and (11), verify that flavicane, and hence stictane triterpenoids, differ from triterpenoids of the oleanane, hopane, and lupane series in their C-8 and C-14 configurations.

Analysis of the methyl group shifts in terms of the $(3\cos^2\theta - 1)r^{-3}$ proportionality now established[7] for lanthanoid-induced shifts, is complicated by the lack of precision surrounding the exact location of the europium

TABLE 3

Chemical shifts (δ) of methyl groups and 17(21)-ene substituent effects (p.p.m.)

Compound	4β	4α	10β	8	14	18	22 *	
21α*H*-Hopane	0.78	0.81	0.84	0.95	0.92	0.64	0.77,	0.87
Hop-17(21)-ene (9a)	0.79	0.83	0.84	0.94	1.05	0.84	0.91,	0.98
17(21)-Ene substituent effect	+0.01	+0.02	0.00	−0.01	+0.13	+0.20		
7β-Acetoxy-21α*H*-hopane	0.80	0.82	0.87	1.08	1.00	0.64	0.78,	0.89
7β-Acetoxyhop-17(21)-ene (9b)	0.78	0.83	0.86	1.07	1.13	0.83	0.90,	0.98
17(21)-Ene substituent effect	−0.02	+0.01	+0.01	−0.01	+0.13	+0.19		
3β-Acetoxyflavicane (2b)	0.86	0.86	0.89	1.14	0.90	0.64	0.79,	0.90
3β-Acetoxyflavic-17(21)-ene (6b)	0.85	0.85	0.94	1.09	0.96	0.81	0.91,	0.97
17(21)-Ene substituent effect	−0.01	−0.01	+0.05	−0.05	+0.06	+0.17		
2α,3β-Diacetoxyflavicane (2d)	0.90	1.03	0.90	1.16	0.90	0.65	0.79,	0.89
2α-3β-Diacetoxyflavic-17(21)-ene (6a)	0.90	1.05	0.95	1.10	0.97	0.82	0.92,	0.98
17(21)-Ene substituent effect	0.00	+0.02	+0.05	−0.06	+0.07	+0.17		
Flavican-3β-ol (2c)	0.78	0.98	0.87	1.14	0.90	0.64	0.79,	0.89
Flavic-17(21)-en-3β-ol (6c)	0.78	0.97	0.91	1.07	0.96	0.80	0.91,	0.98
17(21)-Ene substituent effect	0.00	−0.01	+0.04	−0.07	+0.06	+0.16		

* d, *J* 6—7 Hz.

TABLE 4

Normalized methyl group shifts (p.p.m.)

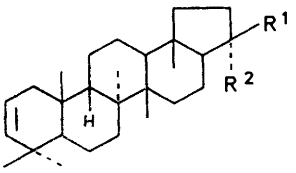
Compound	4β	4α	10β	8	14	18	Other	
Flavican-3β-ol (2c)	10.0	8.95	4.15	1.28	1.10	0.49	0.11	0.09
Flavic-17(21)-en-3β-ol (6c)	10.0	8.95	4.24	1.27	1.20	0.51	0.11	0.04
						C-17	Other	
18α-Oleanan-3β-ol (10)	10.0	9.06	3.97	1.74	0.95	0.55	0.18	0.15
Dammara-20,24-dien-3β-ol (11)	10.0	9.18	3.94	1.72	0.94	0.47	0.19	0.19

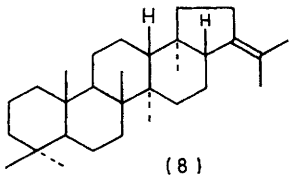
[5] (*a*) C. C. Hinckley, *J. Amer. Chem. Soc.*, 1969, **91**, 5160; (*b*) J. K. M. Sanders and D. H. Williams, *Chem. Comm.*, 1970, 422; (*c*) P. V. Demarco, T. K. Elzay, R. B. Lewis, and E. Wenkert, *J. Amer. Chem. Soc.*, 1970, **92**, 5734, 5737.

[6] D. G. Buckley, G. H. Green, E. Ritchie, and W. C. Taylor, *Chem. and Ind.*, 1971, 298.

[7] A. E. Cockerill, G. L. O. Davies, R. C. Harden, and D. M. Rackham, *Chem. Rev.*, 1973, 567 and references cited therein.

atom relative to the hydroxy oxygen atom. If, in accord with the deductions of other workers,[8] the europium atom is considered to be *ca.* 3.2 Å from the

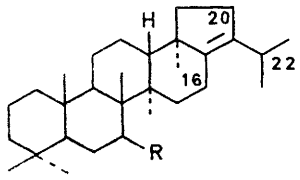


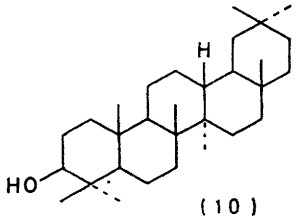


(8)

(7) a; R^1 R^2 = $:CMe_2$

b; H $CHMe_2$

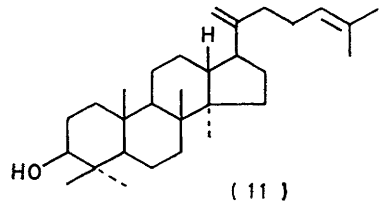




(10)

(9) a; R = H

b; R = OAc



(11)

oxygen atom, and located along a line approximately in the plane of the ring system, then for the essentially planar 3β-alcohols (10) and (11), the angle θ between the oxygen, europium, and methyl group centres is relatively invariant, and in any case small. Thus the $(3\cos^2\theta - 1)$ term can be equated to a constant, and a plot of the normalized shift against r^{-3} should approximate to a straight line. By using methyl to europium atom distances measured from models such a straight line plot is obtained (Figure 2) for compounds (10) and (11), and although this procedure represents an oversimplification of a complex problem, it is apparent that normalized shift data are of value in locating methyl groups relative to a reference 3β-hydroxy-group in triterpenoids such as (10) and (11), which have approximately planar structures.

Neglect of the $(3\cos^2\theta - 1)$ term is, however, often inappropriate. For example Barry *et al.*[8] have noted that in the analysis of the ^1H and ^{13}C n.m.r. spectra of cholesterol, the vinylic protons at C-6 and C-1 are both 6.3 Å from the europium atom, yet the C-1 has three times the induced shift of the C-6 proton. Without some knowledge of the importance of the $(3\cos^2\theta - 1)$ term in the analysis of reference compounds possessing a boat ring B, such as protostan-3β-ols,[9] it is difficult to quantify the effect that this structural feature would have on normalized shifts, especially those of the 8α-methyl groups in (2c) and (6c) for which θ is estimated to be at least 10° greater than θ for any ring B atom in the cholesterol or 18α-oleanan-3β-ol skeletons. Although models indicate that an 8α-methyl group in a flavicane skeleton would be closer to a europium atom than an 8β-methyl group is in 18α-oleanan-3β-ol (10), the observations of Barry *et al.*[8] lead to the conclusion that in the former case, the greater θ value would result in the 8α-methyl group of (2c) or (6c) having an induced shift appreciably smaller than that predicted from distance considerations alone.

In the flavicane skeleton, because of the boat ring B, the molecular framework is bent downwards at the ring BC junction, and in consequence the 14β-methyl group in (2c) would have a smaller θ than that for the 14α-methyl group in (10). Models indicate the europium to C-14 methyl group distances in these compounds to be approximately the same. However the slightly greater normalized shift for the 14β-methyl group in (2c), in comparison with that of the 14α-methyl group in (10) (Table 4), can be rationalized in terms of the lesser value for θ in the former case.

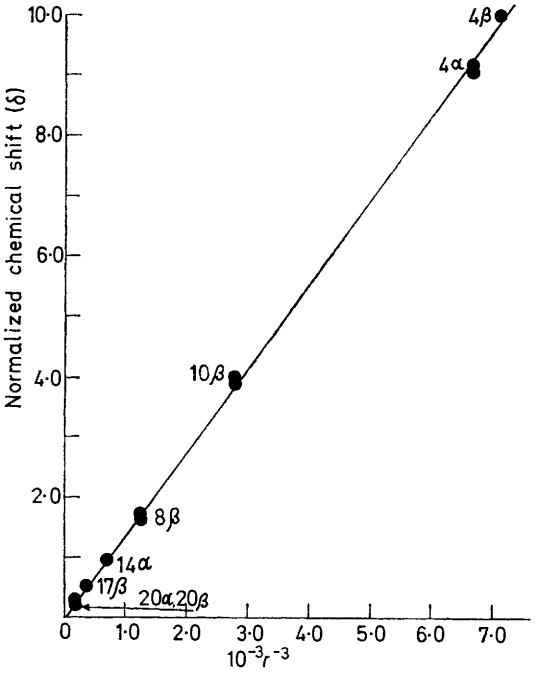


FIGURE 2 Plot of normalized methyl group shifts against 10^{-3} r^{-3} for 18α-oleanan-3β-ol (10) and 3β-hydroxydammara-20,24-diene (11) [r = distance (Å) of methyl group from europium atom]

Models also indicate the C-17 methyl group in (10) and the C-18 methyl group in (2c) and (6c) to be almost equidistant from the 3β-hydroxy-group, and to have

[8] C. D. Barry, C. H. Dobson, D. A. Sweigart, L. E. Ford, and R. J. P. Williams, 'Nuclear Magnetic Shift Reagents,' Academic Press, New York and London, 1973, p. 181.

[9] S. Okuda, Y. Sato, T. Hattori, and H. Igarashi, *Tetrahedron Letters*, 1968, 4769.

similar θ values; hence the similarities in the normalized shifts of these methyl groups are as would be expected. It is also noteworthy that the data (Table 4) for (2c) and (6c) are consistent with the ring E structure proposed previously [1] for stictane (1a), in which a *gem*-dimethyl group is located at C-21 and a methyl group at C-18, rather than an 18α-oleanane type of structure in which the *gem*-dimethyl group is at C-19 and a methyl group at C-17. Ring contraction of a 3β-substituted stictan-22α-ol thus gives flavican-3β-ol derivatives in which the normalized shift of the C-18 methyl group is greater than those of the two more remote secondary methyl groups of the isopropyl group, whereas in lup-20(29)-en-3β-ol, which is a ring-E-contracted 18α-oleanane, the C-17 methyl group has a smaller normalized shift than that of the vinylic methyl group of the pendant isopropenyl group.[6]

The spectral data presented here are consistent with the structures proposed for flavicane (2a) and stictane (1a),[1] and support the conclusion that these structures must differ from the 18α-oleanane type of structure (10) at the BC ring junction, with the chemical shifts of the C-8 and C-14 methyl groups markedly different. The boat ring B, with a β-H at C-9 and an α-Me at C-8 in the stictane and flavicane structures, will account for the observed differences.

EXPERIMENTAL

Experimental procedures are as described in Part VI.[10]

2α,3β-*Diacetoxyflavicane* (2d).—2α,3β-Diacetoxyflavic-22(29)-ene [1] (4a) (100 mg) in AnalaR ethyl acetate (25 ml) was hydrogenated over Adams catalyst for 2 h (uptake 1 mol. equiv.). Removal of the catalyst and evaporation gave 2α,3β-*diacetoxyflavicane* (2d) (95 mg), m.p. 203—205° (from hexane); $\nu_{max.}$ 1 740 and 1 245 cm^{-1} (OAc); δ 1.97 and 2.03 (3 H each, s, OAc), 4.74 (1 H, d, *J* 5 Hz, C*H*·OAc), and 5.16 (1 H, sextet, C*H*·OAc) (Found: C, 77.4; H, 10.7. $C_{34}H_{56}O_4$ requires C, 77.2; H, 10.7%).

2α,3β-*Diacetoxyflavic*-21-*ene* (5) *and* 2α,3β-*Diacetoxyflavic*-22(29)-*ene* (4a).—A solution of 2α,3β-diacetoxystictan-22α-ol (1e) (300 mg) in benzene–hexane (1 : 9; 30 ml) was stirred with an excess of freshly sublimed phosphorus pentachloride (500 mg). After 20 min at room temperature, the mixture was filtered and worked up in the usual way. Separation of the products (280 mg) by multiple (× 2) p.l.c. on silver nitrate-impregnated silica gel with E–H (1 : 9) gave compounds (5) (55 mg) and (4a) (170 mg). 2α,3β-*Diacetoxyflavic*-21-*ene* (5) (higher R_F) had m.p. 180—182° (sublimed sample); $\nu_{max.}$ 1 735 and 1 250 cm^{-1} (OAc); δ 1.56 and 1.72 (3 H each, s, C=C·C*H*$_3$), 1.97 and 2.03 (3 H each, s, OAc), 4.74 (1 H, d, *J* 5 Hz, C*H*·OAc), and 5.16 (1 H, sextet, C*H*·OAc) (Found: C, 77.7; H, 10.5. $C_{34}H_{54}O_4$ requires C, 77.5; H, 10.3%). 2α,3β-Diacetoxyflavic-22(29)-ene (4a) (lower R_F) was identical (m.p. and mixed m.p., i.r. and n.m.r. spectra, and t.l.c.) with an authentic specimen.[1]

2α,3β-*Diacetoxyflavic*-17(21)-*ene* (6a).—(*a*) A solution of 2α,3β-diacetoxyflavic-21-ene (5) (80 mg) and trichloroacetic acid (30 mg) in chloroform (20 ml) was stirred for 24 h at room temperature. The mixture was worked up in the usual way and the products separated by p.l.c. on silver nitrate-impregnated silica gel with E–H (1 : 7) to give as the major product 2α,3β-*diacetoxyflavic*-17(21)-*ene* (6a), m.p. 176—178° (sublimed sample); $\nu_{max.}$ 1 735 and 1 250 cm^{-1} (OAc); δ 1.97 and 2.03 (3 H each, s, OAc), 2.18 and 2.77 (5 H, m, C*H*·C:C), 4.74 (1 H, d, *J* 5 Hz, C*H*·OAc), and 5.16 (1 H, sextet, C*H*·OAc); *m/e* 526 (M^+), 511, 483 (100%), 423, and 363 (Found: C, 77.6; H, 10.4. $C_{34}H_{54}O_4$ requires C, 77.5; H, 10.3%).

(*b*) A solution of 2α,3β-diacetoxyflavic-21-ene (5) (150 mg) in chloroform (9.0 ml) and 98% formic acid (8.1 ml) was kept at 20 °C for 18 h. The red colour that gradually developed was discharged when the mixture was diluted with ether and washed twice with water and then saturated aqueous sodium hydrogen carbonate. Removal of the solvent under reduced pressure and filtration of the product in E–H (1 : 1) through alumina (8 g) gave 2α,3β-diacetoxyflavic-17(21)-ene (6a) (135 mg).

(*c*) A solution of 2α,3β-diacetoxyflavic-22(29)-ene (4a) (150 mg) in chloroform (9.0 ml) and 98% formic acid (8.1 ml) was kept at 20 °C for 24 h. The red colour that gradually developed was discharged when the mixture was diluted with ether and washed twice with water and then with saturated aqueous sodium hydrogen carbonate. Removal of the solvent under reduced pressure and filtration of the product in E–H (1 : 1) through alumina (3 g) gave 2α,3β-diacetoxyflavic-17(21)-ene (6a) (140 mg).

2α,3β-*Diacetoxy*-22-*trichloroacetoxyflavicane* (2e).—A solution of 2α,3β-diacetoxyflavic-22(29)-ene (4a) (50 mg) and trichloroacetic acid (70 mg) in chloroform (15 ml) was stirred for 3 h at 20 °C. The mixture was worked up in the usual way and the products were separated by p.l.c. on silica gel with E–H (1 : 7) to give unchanged (4a) (22 mg) and 2α,3β-*diacetoxy*-22-*trichloroacetoxyflavicane* (2e) (28 mg), $\nu_{max.}$ 1 735, 1 245 (OAc), 1 110, 1 035, 860, 820, and 785 cm^{-1}; δ 0.69 (3 H), 0.89 (9 H), 1.03 (3 H), and 1.15 (3 H) (Me groups), 1.56 (6 H, two s, Me_2C·OR), 1.98 and 2.03 (3 H each, s, OAc), 4.74 (1 H, d, *J* 5 Hz, C*H*·OAc), and 5.16 (1 H, sextet, C*H*·OAc); *m/e* 888 (M^+), 526 (100%), 466, 444, 438, 424, 406, 363, and 328. Sublimation of this compound at 150 °C and 0.01 mmHg gave 2α,3β-diacetoxyflavic-21-ene (5).

Flavic-17(21)-*ene*-2α,3β-*diol* (6d).—A solution of 2α,3β-diacetoxyflavic-17(21)-ene (6a) (500 mg) in ethanolic 2% potassium hydroxide (150 ml) was stirred for 5 h at room temperature. The mixture was worked-up in the usual way and the product, in ether, filtered through alumina (15 g) to give *flavic*-17(21)-*ene*-2α,3β-*diol* (6d) (455 mg), m.p. 220—222° (sublimed sample); $\nu_{max.}$ 3 330 and 3 240 cm^{-1} (OH) (Found: C, 81.6; H, 11.5. $C_{30}H_{50}O_2$ requires C, 81.4; H, 11.4%).

Partial Acetylation of Flavic-17(21)-*ene*-2α,3β-*diol* (6d).—A solution of (6d) (950 mg), in pyridine (80 ml) was stirred with acetic anhydride (2.5 ml) at 20 °C until t.l.c. indicated that optimum monoacetylation had occurred (about 60 min). The mixture was worked up in the usual way and the products separated by multiple (× 2) p.l.c. on silica gel with E–H (1 : 1), to give, in order of decreasing R_F values, compounds (6a) (80 mg), (6e) (390 mg), and (6f) (390 mg), and unchanged diol (6d) (70 mg). 2α-*Acetoxyflavic*-17(21)-*en*-3β-*ol* (6e) had m.p. 216—218° (sublimed sample); δ 0.81 (3 H), 0.85 (3 H), 0.96 (3 H), 1.04 (3 H), 1.08 (3 H), and 0.90 and 1.00 (3 H each, d, *J* 7 Hz) (Me groups), 2.06 (3 H, s, OAc), 3.18 (1 H, d, *J* 5 Hz, C*H*·OH), and 5.00 (1 H, sextet, C*H*·OAc) (Found: C, 79.2; H, 10.9. $C_{32}H_{52}O_3$ requires C, 79.3; H, 10.8%). 3β-*Acetoxyflavic*-17(21)-*en*-2α-*ol* (6f) had m.p. 212—214° (sublimed sample); δ 0.81 (3 H),

[10] Part VI, R. E. Corbett and R. A. J. Smith, *J. Chem. Soc.* (*C*), 1969, 44.

0.87 (6 H), 0.96 (6 H), 1.10 (3 H), and 0.90 and 0.99 (3 H each, d, *J* 7 Hz) (Me groups), 2.11 (3 H, s, OAc), 3.79 (1 H, sextet, C*H*·OAc), and 4.51 (1 H, d, *J* 5 Hz, C*H*·OAc) (Found: C, 79.4; H, 11.0%). Hydrolysis of the diacetate (6a) and the lower R_F value hydroxy-acetate (6f) with ethanolic potassium hydroxide gave the diol (6d). Three repetitions of the partial acetylation cycle gave a 72% overall yield of the higher R_F value hydroxy-acetate (6e).

2α-*Acetoxyflavic*-17(21)-*en*-3-*one* (6g).—A solution of 2α-acetoxyflavic-17(21)-en-3β-ol (6e) (300 mg) in acetone (80 ml) was stirred with a slight excess of Jones reagent. After 3 min at room temperature the mixture was poured into saturated sodium hydrogen carbonate solution and worked up in the usual way. P.l.c. on silica gel with E–H (1 : 4) gave 2α-*acetoxyflavic*-17(21)-*en*-3-*one* (6g) (285 mg), m.p. 204—206° (sublimed sample); $\nu_{max.}$ 1 750, 1 255 (OAc), and 1 710 cm^{-1} (C=O); δ 0.81 (3 H), 0.99 (3 H), 1.08 (3 H), 1.10 (3 H), 1.13 (3 H), 1.19 (3 H), and 0.89 and 0.99 (3 H each, d, *J* 7 Hz) (Me groups), 2.13 (3 H, s, OAc), and 5.60 (1 H, q, C*H*·OAc) (Found: C, 79.7; H, 10.6. $C_{32}H_{50}O_3$ requires C, 79.6; H, 10.4%).

Flavic-17(21)-*en*-3-*one* (6h).—A solution of 2α-acetoxyflavic-17(21)-en-3-one (6g) (500 mg) in toluene (25 ml) was added dropwise over 10 min to a vigorously stirred solution of calcium (1.5 g) in redistilled liquid ammonia (250 ml). After stirring for a further 20 min, bromobenzene was added until the blue colour of the solution was discharged. The ammonia was allowed to evaporate at room temperature and the mixture worked up in the usual way. P.l.c. on silica gel with E–H (1 : 19) gave *flavic*-17(21)-*en*-3-*one* (6h) (385 mg), m.p. 194—195° (sublimed sample); $\nu_{max.}$ 1 705 cm^{-1} (C=O); δ 0.77 (3 H), 0.81 (3 H), 0.98 (3 H), 1.04 (3 H), 1.05 (3 H), 1.13 (3 H), and 0.91 and 0.98 (3 H each, d, *J* 7 Hz) (Me groups) (Found: C, 84.9; H, 11.1. $C_{30}H_{48}O$ requires C, 84.8; H, 11.4%).

Flavic-17(21)-*en*-3β-*ol* (6c).—A solution of flavic-17(21)-en-3-one (6h) (200 mg) in ether (50 ml) was stirred with a slight excess of lithium aluminium hydride for 1 h at 20 °C. The excess of reagent was destroyed with wet ether and the mixture worked up in the usual way. P.l.c. on silica gel with E–H (1 : 3) gave *flavic*-17(21)-*en*-3β-*ol* (6c) (190 mg), m.p. 182—184° (sublimed sample); $\nu_{max.}$ 3 450 cm^{-1} (OH); δ 3.22 (1 H, m, C*H*·OH) (Found: C, 84.6; H, 11.7. $C_{30}H_{50}O$ requires C, 84.4; H, 11.8%).

3β-*Acetoxyflavic*-17(21)-*ene* (6b).—A solution of flavic-17(21)-en-3β-ol (6c) (180 mg) in pyridine (10 ml) was stirred with acetic anhydride (5 ml) for 24 h at room temperature, and the mixture worked up in the usual way. P.l.c. on silica gel with E–H (1 : 9) gave 3β-*acetoxyflavic*-17(21)-*ene* (6b) (175 mg), m.p. 196—197° (sublimed sample); $\nu_{max.}$ 1 730 and 1 240 cm^{-1} (OAc); δ 2.03 (3 H, s, OAc) and 4.50 (1 H, m, C*H*·OAc); *m/e* 468 (M^+, 100%), 453, 425, 408, 393, 365, 191, and 189 (Found: C, 82.2; H, 10.9. $C_{32}H_{52}O_2$ requires C, 82.0; H, 11.2%).

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