β-Tricarbonyl Compounds. Part 1. Synthesis of the Antibiotics Uliginosin A, Dihydrouliginosin B, and Analogues thereof [1]

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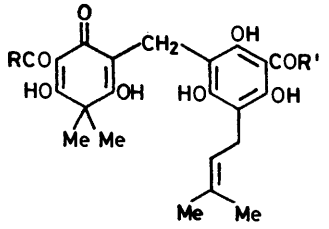
The antibiotic uliginosin A-iBiB has been synthesised by a rottlerone exchange between albaspidin-iBiB and 2',4',6'-trihydroxy-3'-(3-methylbut-2-enyl)isobutyrophenone. Natural uliginosin A contains a homologue (M + 14) and so analogues, in which each of the isobutyryl groups in uliginosin A is replaced by isovaleryl, have been prepared; uliginosin A-iViB is probably the minor component in natural uliginosin A. Dihydrouliginosin B-iBiB and isodihydrouliginosin B-iBiB have also been prepared.

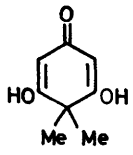
EXTRACTION of the Mexican herb *Hypericum uliginosum* HBK (Tzotzil, 'rabbit plant'), yielded two antibiotics,[2] uliginosin A (1) and uliginosin B (4). The structures were assigned on the basis of spectroscopic evidence [3] and a crystal structure analysis of bromouliginosin B.[4] The close relationship of the antibiotics was shown when acid treatment of uliginosin A afforded a mixture of dihydrouliginosin B (5) and isodihydrouliginosin B (6); the former compound (5) was also obtained by catalytic hydrogenation of uliginosin B. Both uliginosin B [3] and uliginosin A [5] were contaminated with homologues (M + 14) from which they could not be separated by crystallisation. These structures are β-tricarbonyl compounds and, in particular, that of uliginosin A is a hybrid between those of the hop resins [6] and the male fern constituents,[7] which also exist as a mixture of analogues differing only in the nature of the acyl side chain. Whereas the male fern constituents have linear side chains (butyryl, propionyl, and acetyl), the hop

[1] Preliminary communication: T. Meikle and R. Stevens, *J.C.S. Chem. Comm.*, 1972, 123.
[2] H. L. Taylor and R. M. Brooker, *Lloydia*, 1969, **32**, 217.
[3] W. L. Parker and F. Johnson, *J. Amer. Chem. Soc.*, 1968, **90**, 4716.
[4] W. L. Parker, J. J. Flynn, and F. P. Boer, *J. Amer. Chem. Soc.*, 1969, **90**, 4723.
[5] F. Johnson, personal communication.
[6] R. Stevens, *Chem. Rev.*, 1967, **67**, 19.
[7] A. Penttila and J. Sundman, *J. Pharm. Pharmacol.*, 1970, **22**, 393.

resins, kousso resins,[8] and constituents of the essential oil of *Leptospermum flavescens* [9] have branched acyl side chains (isobutyryl, isovaleryl, and 2-methylbutyryl) which are biogenetically related to intermediates in the biosynthesis of valine, leucine, and isoleucine. It therefore seemed probable that in the homologues present in uliginosin A and B one of the two isobutyryl side chains is replaced by isovaleryl.* The impurity present in the natural product is probably either uliginosin A-iViB (2) or uliginosin A-iBiV (3). We report the synthesis of the analogues (1)—(3) and of dihydrouliginosin B-iBiB (5) and isodihydrouliginosin B-iBiB (6).



(1) R = R' = Pr^i
(2) R = Bu^i; R' = Pr^i
(3) R = Pr^i; R' = Bu^i



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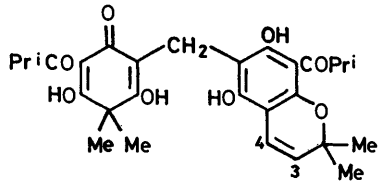
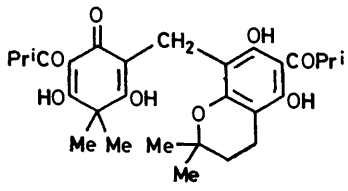


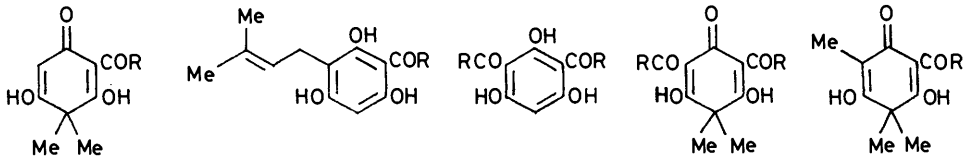
(4)
(5) is 3,4-dihydro-(4)



(6)

Many of the fern constituents have been synthesised by condensing the appropriate monocyclic compound(s) with formaldehyde to form the methylene bridge.[7] To adopt this route to uliginosin A-iBiB (1) it was necessary to prepare isobutyrylfilicinic acid (9) and 2',4',6'-trihydroxy-3'-(3-methylbut-2-enyl)isobutyrophenone (12). For the homologues uliginosin A-iViB (2) and uliginosin A-iBiV (3) isovalerylfilicinic acid (10) and 2',4',6'-trihydroxy-3'-(3-methylbut-2-enyl)isovalerophenone (13) are also required.

Isobutyrylfilicinic acid (9) should be readily available by acylation of filicinic acid and is mentioned in the literature.[10] Filicinic acid (7) has been synthesised by several routes [6,11,12] the most convenient of which [13] involves total *C*-methylation of diacetylphloroglucinol (14) to diacetylfilicinic acid (17) which is subsequently hydrolysed to filicinic acid. Acetylation of phloroglucinol using either acetic acid saturated with boron trifluoride [14] or the commercially available boron trifluoride–acetic acid complex gave diacetylphloroglucinol which was methylated as described [13] to give diacetylfilicinic acid. This method [13] involved the addition of methyl iodide to a methanolic solution of diacetylphloroglucinol and sodium methoxide at 0 °C during 15 min and then further reaction at room temperature during 2 days. We found that if the reaction was worked up after 2 h only 2,4-diacetyl-6-methylphloroglucinol (23) was isolated. If the reaction was carried out without external cooling 2-acetyl-4,4,6-trimethylcyclohexane-1,3,5-trione or a tautomer thereof, *e.g.* (20),



R				
Me (8)	(11)	(14)	(17)	(20)
Pr^i (9)	(12)	(15)	(18)	(21)
Bu^i (10)	(13)	(16)	(19)	(22)

and 2-acetyl-4-methylphloroglucinol (24) were isolated; presumably deacetylation occurs at the higher temperature and the products arise by methylation of the resultant acetylphloroglucinol. In our hands the hydrolysis [12] of diacetylfilicinic acid (17) to filicinic acid (7)

* In the male fern constituents Penttila and Sundman [10] have used suffixes to denote the acyl groups carried by each ring, *i.e.* A = acetyl, B = butyryl, iB = isobutyryl, and iV = isovaleryl. In unsymmetrical methylene bridged compounds the first suffix denotes the acyl group carried by the filicinic acid (7) ring. It is convenient to use this nomenclature to distinguish the analogues of the uliginosins; thus the parent compound becomes uliginosin A-iBiB (1).

[8] M. Lounasmaa, C.-J. Widén, and A. Huhtikangas, *Phytochemistry*, 1973, **12**, 2017; *Acta Chem. Scand.*, 1974, **B28**, 1200, 1209.

[9] I. R. C. Bick, A. J. Blackman, R. O. Hellyer, and D. H. S. Horn, *J. Chem. Soc.*, 1965, 3690.

[10] A. Penttila and J. Sundman, *Acta Chem. Scand.*, 1964, **18**, 344.

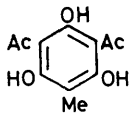
[11] A. Robertson and W. F. Sandrock, *J. Chem. Soc.*, 1933, 1617.

[12] W. Riedl and K. H. Risse, *Annalen*, 1954, **585**, 209.

[13] K. Hoefer and W. Riedl, *Annalen*, 1962, **656**, 127.

[14] T. W. Campbell and G. M. Coppinger, *J. Amer. Chem. Soc.*, 1951, **73**, 2708.

proceeded in poor yield, but with 80% sulphuric acid the monoacetylfilicinic acid (8) was isolated in reasonable



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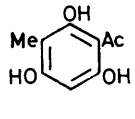
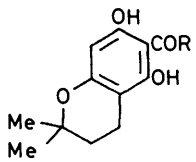


(24)

yield. Accordingly we prepared di-isobutyrylfilicinic acid (18) which on partial hydrolysis gave the required isobutyrylfilicinic acid (9). Heating phloroglucinol with isobutyric acid saturated with boron trifluoride gave a crystalline boron-containing complex which could not be decomposed by treatment with either sodium acetate or boiling aqueous alcohol. It was broken down when an ethereal solution of the complex was washed with portions of aqueous sodium hydroxide. An excess of sodium hydroxide, which would remove the required di-isobutyrylphloroglucinol (15), was indicated by a dramatic change in the colour of the extract, due to the formation of the phenoxide ion. A similar route to diacylphloroglucinols is given in the patent literature [15,16] but no mention is made of the removal of complexed boron. Methylation of di-isobutyrylphloroglucinol (15) to give di-isobutyrylfilicinic acid (18) was carried out at room temperature without significant deacylation, and partial hydrolysis of the product gave the required isobutyrylfilicinic acid (9) in 48% yield. Isovalerylfilicinic acid (10) was prepared in a similar manner but during the methylation of the di-isovalerylphloroglucinol (16) even at 0 °C some deacylation occurred so that the required di-isovalerylfilicinic acid (19) was contaminated with 2-isovaleryl-6-methylfilicinic acid (22). At first this was not realised, and partial hydrolysis of the product gave isovalerylfilicinic acid (10) also contaminated with (22). When this product was condensed with formaldehyde the isovalerylfilicinic acid afforded albaspidin-iViV (28) from which the contaminant (22), which has no free position to condense with formaldehyde, was readily separated. The preparation was therefore repeated and a pure sample of di-isovalerylfilicinic acid (19) obtained by column chromatography and from it pure isovalerylfilicinic acid (10) was prepared. 2-Isobutyryl-6-methylfilicinic acid (21) was not encountered in our work but it has subsequently been prepared as a reference compound in connection with studies of kousso resins.[8]

2′,4′,6′-Trihydroxy-3′-(3-methylbut-2-enyl)isobutyrophenone (12) had not been described in the literature although the di- (deoxycohumulone), tri- (colupulone), and tetra-isoprenylated (colupone) derivatives of 2′,4′,6′-trihydroxyisobutyrophenone and related compounds, *e.g.* (11) and (13), were known from studies on hop resins.[6] It was readily prepared in 54% yield by the addition of 1-bromo-3-methylbut-2-ene to a solution of 2′,4′,6′-trihydroxyisobutyrophenone in 10% potassium hydroxide. However, it was necessary to dry the crude product without the application of heat over sodium hydroxide pellets otherwise cyclisation to a mixture of the isomeric chromans (30) and (33) occurred. Such cyclisations are

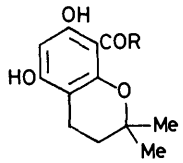


R

Me (29)

Pr^{i} (30)

Bu^{i} (31)



(32)

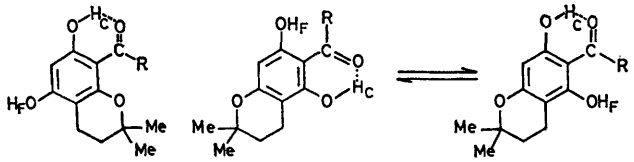
(33)

(34)

known to be catalysed by acids and the same mixture of isomeric chromans was obtained when pure (12) was heated in benzene solution with a trace of toluene-*p*-sulphonic acid. It is probable that crude (12) will contain occluded 1-bromo-3-methylbut-2-ene which on hydrolysis will produce hydrobromic acid to catalyse the cyclisations. The crude product (12) was also contaminated with multi-isoprenylated products but these were removed by washing with cold benzene. The known [17] isovaleryl analogue (13) was prepared in a similar manner but only in 21% yield.

From the mixture of isomeric chromans obtained from (12) in benzene solution, the 8-isobutyrylchroman (33), m.p. 145 °C, crystallised from the cooled solution and the 6-isobutyrylchroman (30), m.p. 142 °C, was obtained from the mother liquors. In agreement with the assigned structures only the 6-isobutyrylchroman (30), which has a free ring position *para* to a phenolic hydroxy, gave a positive reaction with Gibbs reagent.[18] In their u.v. spectra both chromans had $\lambda_{max.}$ at 293—294 nm but on the addition of alkali the 8-isobutyryl isomer (33), which has a free *para*-hydroxy-group, showed a more pronounced bathochromic shift (39 nm) compared with the 6-isomer (30) (10 nm).

The ^{1}H n.m.r. spectra can also distinguish between two such isomers.[19] 8-Acylchromans can only exist as a single chelate (35) whereas 6-acylchromans can exist as



(35) (36) (37)

two distinct enols (36) and (37) which are presumably in equilibrium. The signal from the chelated (H_C)

[15] L. Andersen, Finnish P. 36,700 (*Chem. Abs.*, 1968, **69**, 43,622a).

[16] L. Andersen, R. Lauren, A. Penttila, and J. Sundman, Finnish P. 36,690, 36,691 (*Chem. Abs.*, 1968, **69**, 43,521, 43,522).

[17] W. Riedl, *Chem. Ber.*, 1952, **85**, 692; German P. 899,198 (*Chem. Abs.*, 1958, **52**, 16,300).

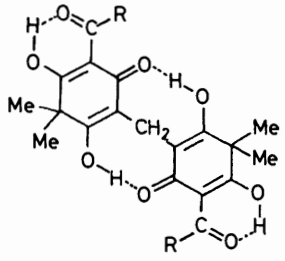
[18] F. E. King, T. J. King, and L. C. Manning, *J. Chem. Soc.*, 1957, 563.

[19] D. J. Ringshaw and H. J. Smith, *Chem. and Ind.*, 1965, 1383.

7-hydroxy proton in (33) was at significantly lower field (τ −4.1) than that (τ −3.7) for the chelated hydroxy-proton in the 6-isobutyrylchroman (30). In both chromans the signal for the unchelated hydroxy-proton (H_F) was at τ 3.09. The signals for the aromatic protons in the two chromans also occur at different field strengths: that in the 6-acylchroman is at higher field (τ *ca.* 4.22) than that in the 8-acylchroman (τ *ca.* 4.05). This is presumably due to shielding by the diamagnetic anisotropy of the fixed pyran ether oxygen in the 6-acyl isomer such as (30). Similar shielding of the aromatic proton in the 8-acyl isomer (33) by the hydroxy-groups at C-5 and C-7 is probably nullified by free rotation. Indeed, the chemical shift for the 6-H proton in 8-isobutyryl-2,2-dimethylchroman-5,7-diol (33) is at τ 3.99 which is virtually the same as that in the 5-*O*-methyl ether (τ 3.98) and the 5,7-dimethyl ether (τ 3.96). Similar arguments have subsequently been applied in assigning the structures (29) and (32) to the acetylchromans [20] and the structures (31) and (34) to the isovalerylchromans.[21]

The synthetic work described below also confirms the assigned structures since the 8-isobutyrylchroman (33) is converted into dihydrouliginosin B-iBiB (5), the structure of which is based on crystal structure analysis of bromouliginosin B.[4]

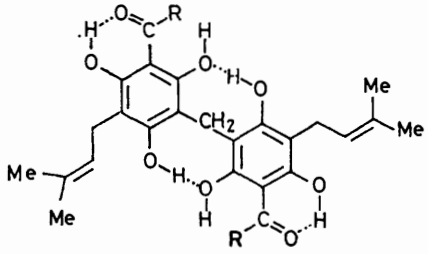
In a slightly alkaline aqueous solution two molecules of an acylfilicinic acid, *e.g.* (8), will condense with formaldehyde to form the symmetrical methylene-bridged albaspidins, *e.g.* (25). By this method the known [10] albaspidin-AA (25) and albaspidin-iBiB (27) and the



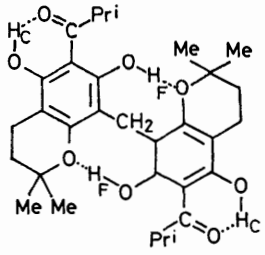
R	
Me	(25)
Pr	(26)
Pri	(27)
Bui	(28)

unknown albaspidin-iViV (28) were prepared. In a similar manner symmetrical methylene-bridged compounds were obtained from 2′,4′,6′-trihydroxy-3′-(3-methylbut-2-enyl)acetophenone (11), 2′,4′,6′-trihydroxy-3′-(3-methylbut-2-enyl)isobutyrophenone (12), the 6- (30) and the 8-isobutyryl-2,2-dimethylchroman-5,7-diols (33). All these symmetrical methylene-bridged compounds (38)—(41) exhibit pronounced lipophilic properties being almost insoluble in methanol and ethanol but readily soluble in benzene and chloroform, except (38) which was only soluble in boiling polar solvents such as dimethylformamide and 2-ethoxyethanol.

The i.r. spectra at low dilution of these compounds indicates that all the carbonyl and hydroxy-groups are



R = Me (38)
Pri (39)



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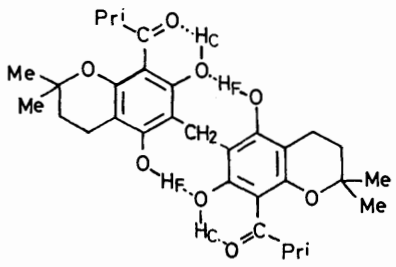


(41)

involved in intramolecular hydrogen bonding, as they are in the uliginosins.[3] In the n.m.r. the chemical shifts of the hydroxy-groups support this conclusion. For example, the free hydroxy-group (OH_F) at position 7 in the 6-isobutyrylchroman (30) is hydrogen-bonded with the pyran oxygen in the second ring in the methylene-bridged compound (40). This means it cannot interfere with the isopropyl group at C-6 which can thus form a stronger chelate with the hydroxy at C-5; the chelated proton at τ −4.00 is now equivalent to that in the 8-isobutyrylchroman (33). In the methylene-bridged compound (41) produced from the 8-isobutyrylchroman (33) the proton (OH_C) is hydrogen bonded with the *ortho*-carbonyl group and appears at τ −6.19. The oxygen in this phenolic group also forms

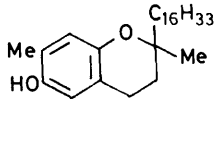
[20] T. Backhouse and A. Robertson, *J. Chem. Soc.*, 1939, 1257; W. J. G. Donnelly and P. V. R. Shannon, *J.C.S. Perkin I*, 1972, 25.

[21] E. K. Pierpoint, A. Robertson, and W. B. Whalley, *J. Chem. Soc.*, 1951, 3104; E. Collins and P. V. R. Shannon, *J.C.S. Perkin I*, 1973, 419.

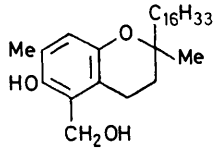
a hydrogen bond with OH_F in the other ring. The signal for this OH_F proton in the bridged compound (41) is at lower field (τ 0.41) than the OH_F proton in the 6-isobutyryl bridged compound (40) (τ 1.07) where it is only hydrogen-bonded to the pyran oxygen.

Many unsymmetrical methylene fern constituents have been synthesised by crossed condensations with formaldehyde but invariably the desired unsymmetrical product is contaminated with the two symmetrical compounds.[7] Nevertheless, we attempted to effect a cross condensation between 6-isobutyrylfilicinic acid (9) and either 2′,4′,6′-trihydroxy-3′-(3-methylbut-2-enyl)-isobutyrophenone (12) or 8-isobutyryl-2,2-dimethylchroman-5,7-diol (33) with formaldehyde in order to prepare uliginosin A-iBiB (1) and dihydrouliginosin B-iBiB (5). In every case only the symmetrical compounds were obtained, and the desired cross condensation products were neither isolated nor detected by t.l.c. Altering the reaction time, the molecular ratio of reactants, and the rate of addition of formaldehyde had no effect on the course of the reaction or the nature of the products. Similar results were obtained with methanol as solvent and using either piperidine or sulphuric acid as catalyst.

Treatment of γ-tocopherol (42) with paraformaldehyde

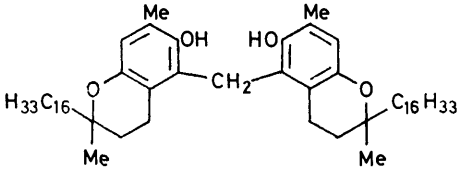


(42)

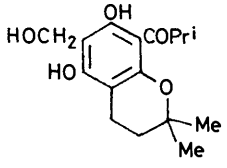


(43)

in the presence of boric and acetic acids gave a hydroxymethylchroman (43) which, on treatment with stronger acids, condensed with a second molecule of γ-tocopherol



(44)



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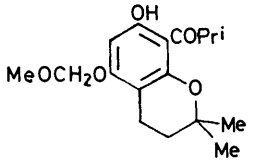
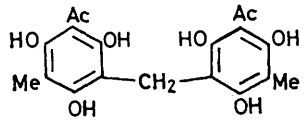


(46)

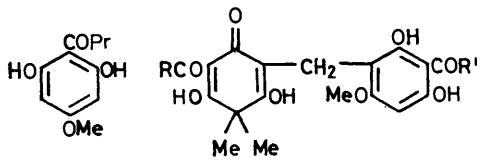
to give the methylene-bridged tocopherol (44).[22] However, all attempts to prepare 6-hydroxymethyl-8-isobutyryl-2,2-dimethylchroman-5,7-diol (45), which with isobutyrylfilicinic acid (9) should give dihydrouliginosin B-iBiB, gave the symmetrical methylene-bridged compound (41). The same compound was also obtained by hydrolysis of 8-isobutyryl 5-methoxymethyleneoxy-2,2-dimethylchroman-7-ol (46). This reaction presumably proceeds *via* the 6-hydroxymethyl compound or free formaldehyde. When the hydrolysis of (46) was repeated in the presence of an excess of isobutyrylfilicinic acid (9) only the symmetrical compound (41) was obtained, but when the hydrolysis of (46) was carried out in the presence of 2′,4′,6′-trihydroxy-3′-methylacetophenone (24) the alternative symmetrical product (47) was obtained. This suggests that the hydrolysis of



(47)

(46) proceeds with the liberation of formaldehyde which condenses more readily with phenols than with enols under these acidic conditions.

A characteristic reaction of asymmetric polyhydroxydiphenylmethanes of the type R^1–CH_2–R^2, known as the rottlerone change,[23] involves their ready disproportionation into two symmetrical diphenylmethanes, R^1–CH_2–R^1 and R^2–CH_2–R^2. If an excess of another 2′,4′,6′-trihydroxyacylphenone, R^3, is present it, too, may enter the ring interchange equilibrium and several fern constituents have been synthesised in this way. For example, heating a mixture of albaspidin BB (26)



(48)

(49) R = R′ = Pr

(50) R = Pr^i; R′ = Pr

and 2′,6′-dihydroxy-4′-methoxybutyrophenone (48) in glacial acetic acid at 80 °C for 1 h afforded deaspidin (49) in 70% yield.[24] However, albaspidin-iBiB (27) and 2′,4′,6′-trihydroxy-3′-(3-methylbut-2-enyl)isobutyrophenone (12) failed to react under these conditions and were recovered unchanged after 18 h at 113 °C; uliginosin A-iBiB was not detected by t.l.c. When the reaction was repeated in 90% acetic acid 2′,4′,6′-trihydroxy-3′-(3-methylbut-2-enyl)isobutyrophenone (12) cyclised to the isomeric chromans (30) and (33), but, in another experiment the 8-isobutyrylchroman (33) failed to react with albaspidin-iBiB (27) to produce dihydrouliginosin B-iBiB. Ring interchange has also occurred

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[23] T. Backhouse, A. McGookin, J. Matchet, A. Robertson, and E. Tittensor, *J. Chem. Soc.*, 1948, 113; A. McGookin, A. Robertson, and T. H. Simpson, *ibid.*, 1951, 2021; 1953, 1828.

[24] A. Penttila and J. Sundman, Finnish P. 36,703 (*Chem. Abs.*, 1968, **69**, 96,266).

in dilute aqueous alkali. For example, in 1% aqueous potassium hydroxide albaspidin-iBiB is reported [25] to react with 2',6'-dihydroxy-4'-methoxybutyrophenone (48) to give deaspidin-iBB (50) but under these conditions albaspidin-iBiB did not react with 2',4',6'-trihydroxy-3'-(3-methylbut-2-enyl)isobutyrophenone (12).

The synthesis of uliginosin A-iBiB (1) was finally achieved when albaspidin-iBiB (27) and 2',4',6'-trihydroxy-3'-(3-methylbut-2-enyl)isobutyrophenone (12) were heated for 90 min in methanol containing sufficient sodium methoxide to form salts with all the non-chelated hydroxy-groups in both reactants. Treatment of the crude reaction product with cold methanol removed the monomeric substances and gave uliginosin A-iBiB (1) in 50% yield. In an analogous manner albaspidin-iBiB and the 8-isobutyrylchroman (33) afforded dihydrouliginosin B-iBiB (5) in 80% yield. Dr. Francis Johnson of the Dow Chemical Company kindly measured the m.p. of the synthetic compounds and the mixed m.p. with the natural products using a differential thermal analysis (D.T.A.) apparatus. Natural and synthetic uliginosin A-iBiB both had m.p. and mixed m.p. 164 °C. Synthetic dihydrouliginosin B-iBiB had m.p. 149 °C whereas the natural product, known [3] to be contaminated with a higher homologue, had m.p. 139 °C; the mixture had m.p. 143 °C.

Attempts to synthesise dihydrouliginosin B-iBiB (5) by the alternative reaction between isobutyrylfilicinic acid (9) and the bischroman (41) failed but albaspidin-iBiB reacted with the 6-isobutyrylchroman (30) to give isodihydrouliginosin B-iBiB (6), m.p. 163 °C in 23% yield. Using a D.T.A. apparatus isodihydrouliginosin-B had m.p. 159 °C, undepressed by the authentic compound supplied by Dr. Johnson. In a similar manner albaspidin-iBiB reacted with 2',4',6'-trihydroxy-3'-(3-methylbut-2-enyl)isovalerophenone (13) to give the homologue uliginosin A-iBiV (3), and albaspidin-iViV (28) reacted with 2',4',6'-trihydroxy-3'-(3-methylbut-2-enyl)isobutyrophenone (12) to give uliginosin A-iViB (2).

The mass spectra of the uliginosins,[3] hop resins,[26] and male fern constituents [27] have been discussed. We examined the mass spectrum of a natural sample of uliginosin A, kindly provided by Dr. F. Johnson, and those of our synthetic analogues (1)—(3), in order to determine the nature of the minor component present in the natural product. An attempt to construct a difference spectrum between natural uliginosin A and synthetic uliginosin A-iBiB (1), normalised with respect to the fragment with *m/e* 500, gave many negative values but suggested that the ions of *m/e* 514, 492, 483, 471, 459, and 412 were due to the other compound. Of these fragments the ions at *m/e* 492, 483, and 412 were not prominent in the mass spectra of either of the analogues (2) or (3) whereas that of *m/e* 459 was present in both. However, the prominent ion of *m/e* 471 is only seen in the spectrum of uliginosin A-iViB (2) where it results from the loss of a propyl radical from the isobutyryl side chain of the phenolic ring. In the middle mass region a significant peak at *m/e* 250 in the spectrum of natural uliginosin A is missing from the synthetic product. Again, this peak is only seen in the mass spectrum of uliginosin A-iViB (2). On the other hand the mass spectrum of uliginosin A-iBiV (3) shows a characteristic ion at *m/e* 291 which is noticeably missing from the spectrum of the natural product. The spectrum of (3) also contains prominent ions at *m/e* 278 and 223. Similar ions, but of much weaker intensity, are seen in the spectra of natural uliginosin A and synthetic uliginosin A-iBiB. These ions are not more intense in the natural product than in synthetic uliginosin A-iBiB so it is unlikely that uliginosin A-iBiV (3) is the natural impurity.

Thus examination of the mass spectra suggests that in the minor component of natural uliginosin A it is the filicinic acid ring that carries the five-carbon acyl side chain. On biogenetic grounds the minor component is probably uliginosin A-iViB (2) but the mass spectra provide no conclusive evidence to confirm this assignment.

Natural uliginosin A and B showed antimicrobial activity against *Staphylococcus aureus* and *Trichophyton mentagrophytes*; uliginosin A being the more active.[2] In a normal screen against *S. aureus*, *Escherichia coli*, *Candida albicans*, and *Mycoplasma galliseptium* none of the synthetic compounds tested showed antimicrobial activity at a concentration of 50 mg ml^{-1}. In a screen against *T. mentagrophytes* in dextrose–peptone–water for 7 days at 25 °C the minimum inhibitory concentrations (mg ml^{-1}) were: uliginosin A-iBiB (1), 25; uliginosin A-iViB (2), 12.5; uliginosin A-iBiV (3), 12.5; and nystatin (a standard antifungal agent), 6.25. Thus, none of the compounds warranted further investigation.

EXPERIMENTAL

I.r. spectra were determined using Unicam SP 200 and Perkin-Elmer 157 instruments and were recorded for Nujol mulls except where stated; major peaks only are recorded. U.v. spectra were determined with Unicam SP 500 and 800 spectrophotometers. ^1H N.m.r. spectra were determined using Perkin-Elmer R12 (60 MHz) and Varian HA-100D (100 MHz) instruments with tetramethylsilane as internal standard. Mass spectra were recorded by P.C.M.U. with an A.E.I. MS 902 spectrometer operating at 70 eV. Preparative t.l.c. was conducted on 100 × 20 cm plates, with 1-mm Kieselgel PF_{254} (Merck) layers. Kieselgel 60 (20—230 mesh) (Merck) was employed for column chromatography. M.p.s are corrected. Where compounds have been claimed to be identical their i.r. spectra were superimposable and mixed m.p.s were not depressed. Light petroleum (b.p. 60—80 °C) was used except where stated.

[25] L. Andersen, A. Penttila, and J. Sundman, Finnish P. 36,705 (*Chem. Abs.*, 1969, **69**, 96263).

[26] S. J. Shaw and P. V. R. Shannon, *Amer. Soc. Brewing Chemists Proc.*, 1969, 5; *Org. Mass Spectrometry*, 1970, **3**, 941; S. J. Shaw, P. V. R. Shannon, and E. Collins, *ibid.*, 1972, **6**, 873.

[27] M. Lounasmaa, A. Karjalainen, C.-J. Widén, and A. Huhtikangas, *Acta Chem. Scand.*, 1971, **25**, 3428, 3441; 1972, **26**, 89; M. Lounasmaa, C.-J. Widén, and T. Reichstein, *Helv. Chim. Acta*, 1973, **56**, 1133.

Anhydrous magnesium sulphate was employed to dry organic solvents and extracts.

Experimental details for the preparation of compounds (38)—(41), (46), and (47), and the detailed mass-spectral patterns of compounds (1)—(3) are deposited as Supplementary Publication No. SUP 22315 (8 pp.).*

Diacetylphloroglucinol (14).—Glacial acetic acid (105 g) was saturated with boron trifluoride at room temperature. To this, or the commercial complex containing 40% (w/w) boron trifluoride (200 ml), was added anhydrous phloroglucinol (50 g) and the mixture heated on a steam-bath for 2 h. After cooling, the mixture was added dropwise to a well stirred solution of potassium acetate (105 g) in water (2.5 l). The precipitated solid, after two recrystallisations from aqueous methanol, gave diacetylphloroglucinol (50 g, 60%) as pale yellow needles, m.p. 168—170 °C (lit.,[14] 168 °C), $\nu_{max.}$ 3 450br, 2 650br, 1 610vbr, 1 300, 1 230, 1 205, 990, 860, and 800 cm^{-1}; τ[$(CD_3)_2CO$] 7.40 (6 H, s, 2 × CO*Me*) and 4.15 (1 H, s, Ar-*H*).

Di-isobutyrylphloroglucinol (15).—Isobutyric acid (100 ml) was saturated with boron trifluoride at room temperature. Anhydrous phloroglucinol (28 g) was added to this complex and the mixture heated on a steam-bath for 2 h and then allowed to cool overnight. The yellow precipitate was dissolved in ether and washed with 5% aqueous sodium hydroxide (100 ml portions) to remove complexed boron. An excess of sodium hydroxide, which would remove the phenol, is indicated by a dramatic change in the colour of the extract due to the formation of the phenoxide ion. Evaporation of the dried ethereal extract gave *di-isobutyrylphloroglucinol* (35 g, 62%) as pale yellow prisms, m.p. 133—135 °C (from cyclohexane) (lit.,[16] 124—127 °C) (Found: C, 63.2; H, 6.7. $C_{14}H_{18}O_5$ requires C, 63.15; H, 6.85%); $\nu_{max.}$ 3 250br, 1 623, 1 200, 1 160, 1 110, 1 030, 990, and 830 cm^{-1}; τ($CDCl_3$) 8.80 (12 H, d, *J* 7 Hz, 2 × COCH*Me*$_2$), 6.02 (2 H, septet, *J* 7 Hz, 2 × COC*H*Me$_2$), 4.16 (1 H, s, Ar-H), and −6.40 (2 H, s, 2 × H-bonded OH).

Di-isovalerylphloroglucinol (16).—Using the procedure described in the previous experiment, anhydrous phloroglucinol (50 g) was acylated with boron trifluoride–isovaleric acid complex (from 250 ml of acid) to give di-isovalerylphloroglucinol (16) (37 g, 32%) as pale yellow prisms, m.p. 117—118 °C (from cyclohexane) (lit.,[28] 114—115 °C) (Found: C, 65.3; H, 7.7. Calc. for $C_{16}H_{22}O_5$: C, 65.25; H, 7.55%); $\nu_{max.}$ 3 400—3 300br, 3 150br, 1 615br, 1 560, 1 300, 1 200, 1 115, 1 050, 940br, and 830 cm^{-1}; τ(CCl_4) 9.00 (12 H, d, *J* 7 Hz, 2 × CH$_2$CH*Me*$_2$), 7.75 (2 H, m, 2 × CH$_2$C*H*Me$_2$), 7.05 (4 H, d, *J* 7 Hz, 2 × COC*H*$_2$), 4.18 (1 H, s, Ar-*H*), and −6.40 (1 H, s, chelated OH).

2,6-*Diacetyl*-4,4-*dimethylcyclohexane*-1,3,5-*trione* (*Diacetylfilicinic Acid*) (17).—Anhydrous diacetylphloroglucinol (40 g) was dissolved in a solution of sodium (17.6 g) in methanol (400 ml) at 0 °C and methyl iodide (36 ml) was added during 15 min while the temperature was held at 0 °C. The mixture was set aside at room temperature for 2 days and then the solvent was evaporated off. The residue was dissolved in ice-cold water (500 ml), acidified with hydrochloric acid, and the tarry solid collected. This crude product was continuously extracted with light petroleum (b.p. 40—60 °C) and the extract was evaporated to dryness to give diacetylfilicinic acid (17) (25 g, 55%), m.p. 60—61 °C after distillation (b.p. 110 °C at 1 mmHg) (lit.,[13] m.p. 65—66 °C); $\nu_{max.}$ 1 670, 1 560br, 1 120, 1 030, 980, 955, and 840 cm^{-1}; τ($CDCl_3$) 8.55 (s) and 8.43 (s) (4.5 : 1, 6 H, CMe$_2$), 7.40 (s) and 7.27 (s) (1 : 1.6, 6 H, 2 × COMe), −8.40 (s), −8.85 (s), and −9.24 (s) (1 : 5 : 5, 2 H, 2 × chelated OH, contributions from tautomers).

2,4-*Diacetyl*-6-*methylphloroglucinol* (23).—The previous reaction was repeated but the product isolated after only 2 h. Treatment of the crude product with cold methanol gave 2,4-diacetyl-6-methylphloroglucinol (23) (8 g, 21%) as pale yellow prisms, m.p. 169—170 °C (from ethyl acetate–light petroleum) (lit.,[29] 160 °C) (Found: C, 58.75; H, 5.55. Calc. for $C_{11}H_{12}O_5$: C, 58.0; H, 5.4%); $\nu_{max.}$ 3 400, 3 200—2 200br, 1 615, 1 575, 1 300, 1 200, 1 100, 990, and 890 cm^{-1}; τ[$(CD_3)_2CO$] 8.00 (3 H, s, Ar*Me*) and 7.40 (6 H, s, 2 × COMe).

Methylation of this compound with dimethyl sulphate and anhydrous potassium carbonate in acetone gave the trimethyl ether as needles, m.p. 67—68 °C (from light petroleum) (lit.,[29] 66—67 °C) (Found: C, 63.45; H, 6.9. Calc. for $C_{14}H_{18}O_5$: C, 63.15; H, 6.8%); $\nu_{max.}$($CHCl_3$) 2 950, 2 870, 1 705, 1 585, 1 460, 1 360, 1 195, 1 150, 1100, and 1 010 cm^{-1}; τ(CCl_4) 7.86 (3 H, s, Ar*Me*), 7.57 (6 H, s, 2 × COMe), and 6.30 (9 H, s, 3 × OMe).

2-*Acetyl*-4,4,6-*trimethylcyclohexane*-1,3,5-*trione* (20).—The previous experiment was repeated at room temperature without external cooling and the product isolated after 2 h. Trituration of the crude product with cold acetone gave 2-acetyl-4,4,6-trimethylcyclohexane-1,3,5-trione (20) (9 g, 22%) as prisms, m.p. 161—162 °C (from ethyl acetate) (lit.,[12] 160—161 °C) (Found: C, 63.0; H, 6.65. Calc. for $C_{11}H_{14}O_4$: C, 62.85; H, 6.7%); $\nu_{max.}$ 3 400—2 500br, 1 660, 1 600br, 1 530, 1 340, 1 280, 1 190, 1 150, and 1 045 cm^{-1}; τ[$(CD_3)_2CO$] 8.67 (3 H, s, =CMe) and 7.50 (3 H, s, COMe). The acetone-soluble material from the previous experiment was recovered and the residue crystallised from water, after decolourising with charcoal, to give 2′,4′,6′-trihydroxy-3′-methylacetophenone (24) (2 g, 6%) as pale yellow needles, m.p. 211 °C (lit.,[30] 210—211 °C); $\nu_{max.}$ 3 500—2 500, 1 630, 1 605, 1 570, 1 300, 1 265, 1 210, and 810 cm^{-1}; τ[$(CD_3)_2CO$] 8.00 (3 H, s, Ar*Me*), 7.35 (3 H, s, COMe), and 3.90 (1 H, s, Ar-H).

2,6-*Di-isobutyryl*-4,4-*dimethylcyclohexane*-1,3,5-*trione* (*Di-isobutyrylfiilicinic Acid*) (18).—Anhydrous di-isobutyrylphloroglucinol (15 g) was dissolved in a solution of sodium (6 g) in ethanol (100 ml) and methyl iodide (105 ml) added during 10 min without external cooling. When the exothermic reaction had subsided the mixture was heated on a steam-bath for 15 min and then evaporated to dryness The residue was dissolved in water (250 ml) and acidified with hydrochloric acid. The precipitate crystallised from methanol to give *di-isobutyrylfilicinic acid* (18) (10.6 g, 64%) as prisms, m.p. 69—70 °C (lit.,[16] 58—60 °C) (Found: C, 65.1; H, 7.4. $C_{16}H_{22}O_5$ requires C, 65.3; H, 7.55%), $\nu_{max.}$($CHCl_3$) 3 500—2 500, 1 670, 1 555br, 1 480, 1 445, 1 370, 1 350, 1 090br, 970, 890, and 825 cm^{-1}; τ($CDCl_3$) 8.80 (6 H, d, *J* 7 Hz, CH*Me*$_2$), 8.76 (6 H, d, *J* 7 Hz, CH*Me*$_2$), 8.54 (s) and 8.41 (s) (3 : 1, 6 H, CMe$_2$), 6.00 (2 H, septet, *J* 7 Hz, 2 × COC*H*Me$_2$), −8.50 (s), −9.1 (s), and −9.55 (s) (1 : 5 : 5, 2 H, chelated OH; contributions from tautomers).

2,6-*Di-isovaleryl*-4,4-*dimethylcyclohexane*-1,3,5-*trione* (19).

* For details see Notice to Authors No. 7, *J.C.S. Perkin I*, 1977, Index issue.

[28] W. J. G. Donnelly and P. V. R. Shannon, *J. Chem. Soc.* (*C*), 1970, 524.

[29] F. H. Dean and A. Robertson, *J. Chem. Soc.*, 1953, 1241.

[30] A. Robertson and W. B. Whalley, *J. Chem. Soc.*, 1951, 3355.

—Anhydrous di-isovalerylphloroglucinol (12 g) was dissolved in a solution of sodium (3.6 g) in ethanol (100 ml) and methyl iodide (8 ml) added over 20 min without cooling. The crude product, isolated as in the previous experiment, was an oil (12 g) which was shown by t.l.c. to be a mixture of two compounds, neither of which was starting material. Chromatography (silica gel, benzene) gave 2,6-*di-isovaleryl*-4,4-*dimethylcyclohexane*-1,3,5-*trione* (19) as an oil (10 g, 76%), b.p. 126—130 °C at 0.5 mmHg (Found: C, 67.15; H, 8.25. $C_{18}H_{26}O_5$ requires C, 67.05; H, 8.15%); $\nu_{max.}$(CCl_4) 1 720, 1 670, 1 540br, 1 470, 1 385, 1 325, 1 225, 1 170, and 1 050 cm^{-1}; τ($CDCl_3$) 9.00 (12 H, d, J 7 Hz, 2 × $COCH_2CHMe_2$), 8.58 (6 H, s, CMe_2), 8.10—7.50 (2 H, m, 2 × $COCH_2CHMe_2$), 7.15 (2 H, d, J 7 Hz, $COCH_2CHMe_2$), 7.00 (2 H, d, J 7 Hz, $COCH_2CHMe_2$), —8.20 (s), —8.70 (s), and —9.10 (s) (1 : 5 : 5, 2 H, chelated OH; contributions from tautomers).

2-*Acetyl*-4,4-*dimethylcyclohexane*-1,3,5-*trione* (8).—2,6-Diacetyl-4,4-dimethylcyclohexane-1,3,5-trione (17) (14 g) was heated in 80% sulphuric acid (14 ml) on a steam-bath for 40 min. The mixture was then poured with vigorous stirring onto crushed ice (100 g) and the liberated solid crystallised from ethyl acetate to give the monoacetylfilicinic acid (8) (3.2 g, 28%) as white prisms, m.p. 174—175 °C (lit.,[12] 174—176 °C); $\nu_{max.}$ 2 700, 2 650, 1 623, 1 560br, 1 320, 1 255, 1 175, and 850 cm^{-1}; τ[$(CD_3)_2CO$] 8.62 (6 H, s, CMe_2), 7.50 (3 H, s, COMe), 4.50 (1 H, s, 6-H), —8.50 (1 H, s, chelated OH).

2-*Isobutyryl*-4,4-*dimethylcyclohexane*-1,3,5-*trione* (9).—2,6-Di-isobutyryl-4,4-dimethylcyclohexane-1,3,5-trione (18) (3 g) was heated in 80% sulphuric acid (3 ml) on a steam-bath for 40 min and then poured, with vigorous stirring, onto crushed ice (25 g). The liberated solid (2 g) was crystallised from benzene to give the required *monoisobutyrylfilicinic acid* (9) (1.1 g, 48%) as prisms, m.p. 153—155 °C (lit.,[16] 148—150 °C) (Found: C, 64.45; H, 7.15. $C_{12}H_{16}O_4$ requires C, 64.3; H, 7.2%), $\nu_{max.}$ 3 500—2 200, 1 635, 1 550br, 1 245, 1 175, 955, 850, and 835 cm^{-1}; τ[$(CD_3)_2CO$] 8.90 (6 H, d, J 7 Hz, $COCHMe_2$), 8.62 (6 H, s, CMe_2), 6.02 (1 H, septet, J 7 Hz, $COCHMe_2$), 4.50 (1 H, s, 6-H), —8.70 (1 H, s, chelated OH). Evaporation of the mother liquor gave unchanged starting material (0.8 g).

2-*Isovaleryl*-4,4-*dimethylcyclohexane*-1,3,5-*trione* (10).—2,6-Di-isovaleryl-4,4-dimethylcyclohexane-1,3,5-trione (19) (10 g) in 80% sulphuric acid (10 ml) was heated at 60 °C for 5 h. The cooled solution was poured, with vigorous stirring, onto crushed ice (75 g) and the crude product extracted into ether. The extract was washed with water and aqueous sodium hydrogencarbonate, dried, and evaporated to dryness. The residue crystallised from light petroleum to give the *monoisovalerylfilicinic acid* (10) (2 g, 27%) as prisms, m.p. 99—100 °C (Found: C, 65.35; H, 7.6. $C_{13}H_{18}O_4$ requires C, 65.5; H, 7.6%), $\nu_{max.}$ 3 500—3 100, 1 635, 1 540br, 1 310, 1 250, 1 180, 1 080, 970, 860, and 835 cm^{-1}; τ[$(CD_3)_2CO$] 9.05 (6 H, d, J 7 Hz, $COCH_2CHMe_2$), 8.66 (6 H, s, CMe_2), 8.3—7.5 (1 H, m, $COCH_2CHMe_2$), 7.19 (2 H, d, J 7 Hz, $COCH_2CHMe_2$), 4.59 (1 H, s, 6-H), and —8.40 (1 H, s, chelated OH).

2′,4′,6′-*Trihydroxy*-3′-(3-*methylbut*-2-*enyl*)*isobutyrophenone* (12).—1-Bromo-3-methylbut-2-ene (36 g) was added during 1.5 h to a vigorously stirred, ice-cold solution of anhydrous 2′,4′,6′-trihydroxyisobutyrophenone[31] (40 g) in 10% aqueous potassium hydroxide (200 ml) containing crushed ice. The yellow precipitate was collected, washed with water, and dried in a vacuum desiccator containing both concentrated sulphuric acid and solid sodium hydroxide. The dried product was washed thoroughly with cold benzene, and crystallised from benzene to give 2′,4′,6′-*trihydroxy*-3′-(3-*methylbut*-2-*enyl*)*isobutyrophenone* (12) (35 g, 54%) as yellow prisms, m.p. 166 °C (Found: C, 67.9; H, 7.7. $C_{15}H_{20}O_4$ requires C, 68.15; H, 7.65%); $\nu_{max.}$ 3 500, 3 400, 1 645, 1 615, 1 250db, 1 180, 1 140, 1 100, 1 070, and 830 cm^{-1}; τ[$(CD_3)_2CO$)] 8.85 (6 H, d, J 7 Hz, $COCHMe_2$), 8.35 (3 H, s, =CMe), 8.24 (3 H, s, =CMe), 6.72 (2 H, d, J 7 Hz, $ArCH_2$), 5.97 (1 H, septet, J 7 Hz, $COCHMe_2$), 4.72 (1 H, t, J 7 Hz, $CH{=}CMe_2$), 3.89 (1 H, s, Ar-H).

2′,4′,6′-*Trihydroxy*-3′-(3-*methylbut*-2-*enyl*)*isovalerophenone* (13).—Anhydrous 2′,4′,6′-trihydroxyisovalerophenone (21 g), in 10% aqueous potassium hydroxide solution (98 ml), was heated with 1-bromo-3-methylbut-2-ene (17.9 g) as described previously. The crude product, isolated in a similar manner, crystallised from benzene to give 2′,4′,6′-trihydroxy-3′-(3-methylbut-2-enyl)isovalerophenone (13) (6 g, 21%) as pale yellow prisms, m.p. 138—139 °C (lit.,[17] 138.5—140 °C); $\nu_{max.}$ 3 300, 3 500—2 300, 1 620, 1 315, 1 290, 1 230, 1 205, 1 105, 1 075, and 815 cm^{-1}; τ[$(CD_3)_2CO$] 9.05 (6 H, d, J 7 Hz, $COCH_2CHMe_2$), 8.35 (s) and 8.25 (s) (6 H, $=CMe_2$), 8.15—7.40 (1 H, m, $COCH_2CHMe_2$), 7.05 (2 H, d, J 7 Hz, $COCH_2CHMe_2$), 6.75 (2 H, d, J 7 Hz, $ArCH_2$), 4.75 (1 H, t, J 7 Hz, $CH_2CH{=}CMe_2$), 3.95 (1 H, s, Ar-H), 1.10 (1 H, s, OH), 0.65 (1 H, s, OH), —3.95 (1 H, s, H-bonded OH).

5,7-*Dihydroxy*-6-*isobutyryl*-2,2-*dimethylchroman* (30) *and* 5,7-*Dihydroxy*-8-*isobutyryl*-2,2-*dimethylchroman* (33).—Crude, benzene-washed 2′,4′,6′-trihydroxy-3′-(3-methylbut-2-enyl)-isobutyrophenone (12) (37 g) and toluene-*p*-sulphonic acid (0.1 g) were heated under reflux in benzene (100 ml) until the phenol dissolved. On cooling this solution the 8-*isobutyrylchroman* (33) (15 g, 40%) separated as yellow prisms, m.p. 145—146 °C (from benzene–cyclohexane) (Found: C, 68.4; H, 7.7. $C_{15}H_{20}O_4$ requires C, 68.15; H, 7.65%); $\lambda_{max.}$ (acid EtOH) 228sh and 294 nm (ε 17 000), $\lambda_{max.}$ (alkaline EtOH) 245 (8 100), and 332 nm (ε 29 200); $\nu_{max.}$ 3 500br, 1 625, 1 603, 1 523, 1 423, 1 260, 1 230, 1 160, 1 140, 1 120, 1 110, 1 090, 1 000, and 835 cm^{-1}; τ($CDCl_3$) 8.84 (6 H, d, J 6.6 Hz, $CHMe_2$), 8.60 (6 H, s, CMe_2), 8.22 (2 H, t, J 6.6 Hz, 3-CH_2), 7.40 (2 H, t, J 6.6 Hz, 4-CH_2), 6.12 (1 H, septet, J 6.6 Hz, $COCHMe_2$), 3.99 (1 H, s, Ar-H), 3.02 (1 H, s, 5-OH), and —4.10 (1 H, s, 7-OH); τ[$(CD_3)_2CO$] 8.85 (6 H, d, J 6.6 Hz, $CHMe_2$), 8.60 (6 H, s, CMe_2), 8.21 (2 H, t, J 6.6 Hz, 3-CH_2), 7.40 (2 H, t, J 6.6 Hz, 4-CH_2), 6.10 (1 H, septet, J 6.6 Hz, $COCHMe_2$), 4.01 (1 H, s, Ar-H), and —3.75 (1 H, s, 7-OH). Evaporation of the filtrate gave a yellow solid which was continuously extracted with light petroleum (b.p. 40—60 °C). Evaporation of the solvent gave the 6-isobutyrylchroman (30) contaminated with a small amount of the 8-isobutyryl isomer (33). Crystallisation from carbon tetrachloride gave pure 5,7-*dihydroxy*-6-*isobutyryl*-2,2-*dimethylchroman* (30) as yellow plates, m.p. 142—143 °C (Found: C, 68.0; H, 7.55. $C_{15}H_{20}O_4$ requires C, 68.15; H, 7.65%), $\lambda_{max.}$ (acid EtOH) 228 (14 500) and 293 nm (ε 20 200), $\lambda_{max.}$ (alkaline EtOH) 244 (sh), 303 (19 200), and 375 nm (ε 5 000); $\nu_{max.}$ 3 225br, 1 625, 1 590, 1 560, 1 245, 1 230, 1 165, 1 120, 1 100, 1 075, and 820 cm^{-1}; τ($CDCl_3$) 8.80 (6 H, d, J 6.6 Hz, $CHMe_2$), 8.69 (6 H, s, CMe_2), 8.22 (2 H, t, J 6.6 Hz, 3-CH_2), 7.40 (2 H, t, J 6.6 Hz, 4-CH_2), 6.05 (1 H, septet, J 6.6 Hz,

[31] G. A. Howard, J. R. A. Pollock, and A. R. Tatchell, *J. Chem. Soc.*, 1955, 174.

COC*H*Me$_2$), 4.22 (1 H, s, Ar-H), 3.09 (1 H, s, OH), and −3.70 (1 H, s, chelated OH).

5,7-Dihydroxy-6-isovaleryl-2,2-dimethylchroman (31) *and 5,7-Dihydroxy-8-isovaleryl-2,2-dimethylchroman* (34).—Crude, benzene-washed, 2′,4′,6′-trihydroxy-3′-(3-methylbut-2-enyl)isovalerophenone (13) (5 g) and toluene-*p*-sulphonic acid (0.05 g) were heated under reflux in benzene (25 ml) until the phenol dissolved. On cooling this solution the 8-isovalerylchroman (2 g, 40%) separated as small yellow prisms, m.p. 135—136 °C (from cyclohexane) (lit.,[21] m.p. 138 °C) (Found: C, 68.9; H, 7.8. Calc. for $C_{16}H_{22}O_4$: C, 69.05; H, 7.95%); $\nu_{max.}$(CHCl$_3$) 3 550, 3 200br, 1 610, 1 490, 1 415, 1 365, 1 150, 1 120, 1 080, and 885 cm^{-1}; τ(CDCl$_3$) 9.04 (6 H, d, *J* 6.6 Hz, COCH$_2$CH*Me*$_2$), 8.62 (6 H, s, CMe$_2$), 8.24 (2 H, t, *J* 6.6 Hz, 3-CH$_2$), 8.2—7.5 (1 H, m, COCH$_2$C*H*Me$_2$), 7.4 (2 H, t, *J* 6.6 Hz, 4-CH$_2$), 7.08 (2 H, d, *J* 6.6 Hz, COC*H*$_2$), 4.04 (1 H, s, Ar-H), and −4.02br (1 H, s, 7-OH). Evaporation of the filtrate gave a yellow solid (3 g) which was shown by t.l.c. to be a mixture of the two isomeric chromans. A portion (0.5 g) of this material was chromatographed on a column of silica gel. The fraction eluted by toluene gave the 6-isovalerylchroman (31) (0.15 g) as pale yellow needles, m.p. 141—142 °C (from cyclohexane) (lit.,[12] m.p. 142 °C) (Found: C, 69.3; H, 7.95. Calc. for $C_{16}H_{22}O_4$: C, 69.05; H, 7.95%); $\nu_{max.}$(CHCl$_3$) 3 550, 3 240br, 1 625, 1 595, 1 425, 1 300, 1 160, 1 120, 1 075, and 885 cm^{-1}; τ(CDCl$_3$) 9.03 (6 H, d, *J* 6.6 Hz, CH*Me*$_2$), 8.68 (6 H, s, CMe$_2$), 8.24 (2 H, t, *J* 6.6 Hz, 3-CH$_2$), 8.0—7.5 (1 H, m, C*H*Me$_2$), 7.40 (2 H, t, *J* 6.6 Hz, 4-CH$_2$), 7.04 (2 H, d, *J* 7 Hz, COC*H*$_2$), 4.22 (1 H, s, Ar-H), 2.75 (1 H, s, OH), and −3.59 (1 H, s, chelated OH). Further elution with ether gave the 8-isovalerylchroman (0.25 g), identical with the sample isolated above.

Albaspidin-iBiB (26).—Formalin (40%) (0.8 ml) was added to a stirred solution of 2-isobutyryl-4,4-dimethylcyclohexane-1,3,5-trione (4.5 g) in 1% aqueous potassium hydroxide (120 ml). The mixture was kept at room temperature for 15 min and then acidified with hydrochloric acid. The precipitate was crystallised from ethanol to give albaspidin-iBiB (26) (2 g, 44%) as prisms, m.p. 168—169 °C (lit.,[10] 168—169 °C); $\nu_{max.}$ 2 600br, 1 640, 1 570, 1 325, 1 300, 1 200, 1 090, 925, and 850 cm^{-1}; τ(CCl$_4$) 8.85 (12 H, d, *J* 7 Hz, 2 × CH*Me*$_2$), 8.51 (s) and 8.48 (s) (12 H, 2 × CMe$_2$), 6.70 (2 H, s, CH$_2$), 5.8 (2 H, septet, *J* 7 Hz, 2 × COC*H*Me$_2$), −2.15 (2 H, s, 2 × OH), and −8.80 (2 H, s, 2 × chelated OH).

Albaspidin-iViV (28).—In a similar manner 2-isovaleryl-4,4-dimethylcyclohexane-1,3,5-trione (4 g) was condensed with 4% formalin (6.5 ml) in 1% aqueous potassium hydroxide solution (100 ml) to give *albaspidin-iViV* (28) (1.9 g, 47%) as plates, m.p. 133—134 °C (from methanol) (Found: C, 66.45; H, 7.35. $C_{27}H_{36}O_8$ requires C, 66.35; H, 7.45%); $\nu_{max.}$ 3 300—2 300, 1 640, 1 560, 1 290, 1 205, and 865 cm^{-1}; τ(CCl$_4$) 8.99 (12 H, d, *J* 7 Hz, 2 × CH*Me*$_2$), 8.51 (s) and 8.48 (s) (12 H, 2 × CMe$_2$), 7.80 (2 H, m, 2 × C*H*Me$_2$), 6.98 (4 H, d, *J* 7 Hz, 2 × COC*H*$_2$CHMe$_2$), 6.75 (2 H, s, bridging CH$_2$), −2.10 (2 H, s, 2 × OH), and −8.60 (2 H, s, 2 × chelated OH).

Uliginosin A-iBiB (1).—Sodium hydride (0.25 g), albaspidin-iBiB (27) (0.92 g), and 2′,4′,6′-trihydroxy-3′-(3-methylbut-2-enyl)isobutyrophenone (12) (1 g) were heated under reflux in methanol (10 ml) for 1.5 h. The solvent was evaporated off and the residue dissolved in water (50 ml) and acidified with hydrochloric acid. The liberated oil was extracted into chloroform (2 × 25 ml), washed with water (2 × 25 ml), and dried. Evaporation of the chloroform gave a yellow gum which, on treatment with cold methanol, afforded *uliginosin A-iBiB* (1) (0.5 g, 50%) as yellow prisms, m.p. 161—162 °C (from acetonitrile–chloroform, 9 : 1) (lit.,[3] 160.5—161.5 °C) (Found: C, 66.95; H, 7.3. $C_{28}H_{36}O_8$ requires C, 67.2; H, 7.25%); $\lambda_{max.}$ (cyclohexane) 229 (34 000) and 294 nm (ε 26 000); $\nu_{max.}$(CCl$_4$) 3 350, 3 150, 2 950, 2 920, 2 900 (sh), 2 650, 1 640, 1 613, 1 580, 1 535, 1 480, 1 440, 1 390, 1 360, 1 295, 1 265, 1 195, 1 095, and 920 cm^{-1}; τ(CCl$_4$) 8.85 (d, *J* 7 Hz) and 8.84 (d, *J* 7 Hz) (12 H, 2 × CH*Me*$_2$), 8.65 (weak s), 8.50 (s) (6 H, CMe$_2$), 8.20 (3 H, s, CH=C*Me*), 8.13 (3 H, s, CH=C*Me*), 6.63 (weak s), 6.52 (s), 6.13 (septet, *J* 7 Hz), and 5.83 (septet, *J* 7 Hz) (6 H, C*H*$_2$CH=CMe$_2$ + bridging CH$_2$ + 2 × COC*H*Me$_2$), 4.76 (1 H, t, *J* 7 Hz, C*H*=CMe$_2$), 3.80br (1 H, s, OH), −0.10 (1 H, s, OH), −1.15br (1 H, s, OH), −6.21 (1 H, s, OH), and −8.78 (1 H, s, OH).

Uliginosin A-iViB (2).—Sodium hydride (0.14 g), albaspidin-iViV (28) (0.49 g), and 2′,4′,6′-trihydroxy-3′-(3-methylbut-2-enyl)isobutyrophenone (12) (0.53 g) were heated under reflux in methanol (10 ml) for 1.5 h. The crude product, isolated as before, gave the homologue *uliginosin A-iViB* (2) (0.38 g, 74%) as yellow prisms, m.p. 157—158 °C (from acetonitrile) (Found: C, 67.75; H, 7.25. $C_{29}H_{38}O_8$ requires C, 67.65; H, 7.45%); $\nu_{max.}$(CCl$_4$) 3 500—2 300, 1 640, 1 610, 1 580, 1 480, 1 440, 1 385, 1 265, 1 200, and 925 cm^{-1}, τ(CCl$_4$) 8.97 (6 H, d, *J* 7 Hz, COCH$_2$CH*Me*$_2$), 8.85 (6 H, d, *J* 7 Hz, COCH*Me*$_2$), 8.65 (weak s) and 8.50 (s) (6 H, CMe$_2$), 8.15br (6 H, s, CH$_2$CH=C*Me*$_2$), 8.0—7.30 (1 H, m, COCH$_2$C*H*Me$_2$), 6.95 (2 H, d, *J* 7 Hz, COC*H*$_2$CHMe$_2$), 6.75—6.40 (4 H, m, C*H*$_2$CH=CMe$_2$ + bridging CH$_2$), 6.15 (1 H, septet, *J* 7 Hz, COC*H*Me$_2$), 4.80 (1 H, t, *J* 7 Hz, CH$_2$C*H*=CMe$_2$), 3.80 (1 H, s, OH), −0.10 (1 H, s, OH), −1.15 (1 H, s, OH), −6.25 (1 H, s, OH), and −8.65 (1 H, s, OH).

Uliginosin A-iBiV (3).—Sodium hydride (0.14 g), albaspidin-iBiB (0.46 g), and 2′,4′,6′-trihydroxy-3′-(3-methylbut-2-enyl)isovalerophenone (13) (0.56 g) were heated under reflux in methanol (10 ml) for 1.5 h. The crude product, isolated as above, gave *uliginosin A-iBiV* (3) (0.3 g, 59%) as yellow prisms, m.p. 140.5—142 °C (from acetonitrile) (Found: C, 67.9; H, 7.45%; *M*$^+$ 514.255 4. $C_{29}H_{38}O_8$ requires C, 67.65; H, 7.45%; *M*, 514.256 7); $\nu_{max.}$(CCl$_4$) 3 500—2 300, 1 640, 1 610, 1 585, 1 480, 1 435, 1 370, 1 310, 1 200, 1 100, and 920 cm^{-1}; τ(CCl$_4$) 9.01 (6 H, d, *J* 7 Hz, COCH$_2$CH*Me*$_2$), 8.82 (6 H, d, *J* 7 Hz, COCH*Me*$_2$), 8.65 (weak s) and 8.51 (s) (6 H, CMe$_2$) and 8.13 (s) (6 H, CH=C*Me*$_2$), 8.05—7.35 (1 H, m, CH$_2$C*H*Me$_2$), 7.09 (2 H, d, *J* 7 Hz, COC*H*$_2$CHMe$_2$), 6.68—6.45 (4 H, m, C*H*$_2$CH=CMe$_2$ + bridging CH$_2$), 5.90 (1 H, septet, *J* 7 Hz, COC*H*Me$_2$), 4.80 (1 H, t, *J* 7 Hz, C*H*=CMe$_2$), 3.85 (1 H, s, OH), −0.15 (1 H, s, OH), −1.20 (1 H, s, OH), −6.25 (1 H, s, OH), and −8.80 (1 H, s, OH).

Dihydrouliginosin B (5).—Sodium hydride (0.19 g), 5,7-dihydroxy-8-isobutyryl-2,2-dimethylchroman (33) (1 g), and albaspidin-iBiB (26) (0.92 g) were heated under reflux in ethanol (10 ml) for 45 min. The crude product was isolated as in the previous experiments and on treatment with cold methanol gave *dihydrouliginosin B* (5) (0.83 g, 83%) as yellow prisms, m.p. 141—142 °C (from acetonitrile–chloroform 9 : 1) (lit.,[3] 138—141 °C) (Found: C, 67.3; H, 7.2. $C_{28}H_{36}O_8$ requires C, 67.2; H, 7.25%); $\lambda_{max.}$ (cyclohexane) 232 (28 600) and 298 nm (ε 24 800); $\nu_{max.}$(CCl$_4$) 3 150br, 2 980, 2 940, 2 870, 1 640, 1 605, 1 580, 1 480, 1 425, 1 385, 1 370, 1 355, 1 275, 1 195, 1 160, 1 140,

1 120, 1 045, and 915 cm^{-1}; τ(CCl_4) 8.83 (d, *J* 6.5 Hz) and 8.81 (d, *J* 6.5 Hz) (12 H, 2 × COCH*Me*$_2$), 8.62 (s) and 8.50 (s) (12 H, $OCMe_2$ and CMe_2), 8.24 (2 H, t, *J* 6.5 Hz, chroman 3-CH_2), 7.37 (2 H, t, *J* 6.5 Hz, chroman 4-CH_2), 6.52 (2 H, s, bridging CH_2), 6.18 (septet) and 5.80 (septet) (2 H, *J* 6.5 Hz, 2 × COC*H*Me_2), −0.17 (1 H, s, OH), −1.00 (1 H, s, OH), −6.53 (1 H, s, OH), and −8.77 (1 H, s, OH).

Isodihydrouliginosin B (6).—Sodium hydride (0.22 g), 5,7-dihydroxy-6-isobutyryl-2,2-dimethylchroman (30) (1.19 g), and albaspidin-iBiB (27) (1.38 g) were heated under reflux in ethanol (10 ml) for 1 h. The product, isolated as above, gave *isodihydrouliginosin B* (6) (0.7 g, 23%) as pale yellow prisms, m.p. 163 °C (from acetonitrile–chloroform 4 : 1) (lit.,[3] 156—158 °C) (Found: C, 66.95; H, 7.1. $C_{28}H_{36}O_8$ requires C, 67.2; H, 7.25%), $\lambda_{max.}$ (cyclohexane) 231 (27 500) and 283 nm (ε 23 000); $\nu_{max.}$(CCl_4) 3 200, 2 150, 2 650, 2 970, 2 920, 2 870, 1 640, 1 610, 1 480, 1 430, 1 380, 1 350, 1 280, 1 255, 1 230, 1 185, 1 150, 1 135, 1 110, and 980 cm^{-1}; τ(CCl_4) 8.82 (d, *J* 6.6 Hz) and 8.80 (d, *J* 6.6 Hz) (12 H, 2 × COCH*Me*$_2$), 8.53 (s) and 8.49 (s) (12 H, $OCMe_2$ + CMe_2), 8.29 (2 H, t, *J* 6.6 Hz, chroman 3-CH_2), 7.40 (2 H, t, *J* 6.6 Hz, chroman 4-CH_2), 6.55 (2 H, s, bridging CH_2), 5.90 (2 H, 2 septets, *J* 6.6 Hz, 2 × COC*H*Me_2), 0.75 (1 H, s, OH), −1.00 (1 H, s, OH), −4.08 (1 H, s, OH), and −8.85 (1 H, s, OH).

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