Fungal Metabolites. Part 15.[1] Structure and Chemical Correlations of Uvidin C, D, and E, New Drimane Sesquiterpenes from *Lactarius uvidus* Fries

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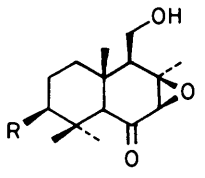
Uvidin C (3), uvidin D (6), and uvidin E (10) have been isolated from *Lactarius uvidus* Fries (Basidiomycetes). The structures, including the absolute stereochemistry, of these three uvidins have been determined by spectroscopic data and chemical correlations with the known (+)-uvidin A (1).

Lactarius species (Russulaceae, Basidiomycetes) are known to produce a variety of compounds, including guaiane,[2] lactarane,[2] marasmane,[2,3] isolactarane,[2] and caryophillane[4] sesquiterpenes, and chromenes.[5] *Lactarius uvidus* Fries represents one of the few species among Basidiomycetes that produce sesquiterpenes with the bicyclofarnesane skeleton, while it remains unique in the Russulaceae family. We have previously reported the isolation and structure determination of the new drimanes uvidin A (1) and uvidin B (2), which along with drimenol, are the main constituents of an acetone extract of *L. uvidus*.[6] G.c.–m.s. analysis of an acetone extract indicated, in addition to (1) and (2), some minor sesquiterpenes of *L. uvidus* with intermediate polarity.[6] Thus, from the column chromatography fractions between those of (1) and (2) we could isolate three new sesquiterpenes in very small amounts.

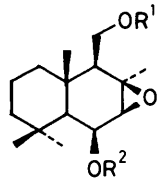
In this paper we describe the isolation and structure elucidation of these new metabolites, namely uvidin C (3), uvidin D (6), and uvidin E (10). A few more related sesquiterpenes were also partially purified, but their structures could not be established because of the poor amounts available.

Uvidin C (3), plates from hexane, m.p. 110—112 °C (M^+, 254), showed spectral features consistent with the presence of one secondary and one primary free hydroxy group, one epoxide group, and four tertiary methyl groups. Reaction of compound (3) with Ac_2O–pyridine afforded the monoacetyl derivative (4), while acetylation of the secondary OH was rather slow and required 4-dimethylaminopyridine as catalyst to afford (5). In the ^1H n.m.r. spectrum of compound (5) the signal for the C*H*OAc appeared as a doublet of doublets, being coupled with the methine of the epoxy ring (J 6.0 Hz) and with a proton resonating at δ *ca.* 1.00, presumably the 5-H.†,‡ These data strongly suggested that the structure of '6-dihydrouvidin A' could be assigned to uvidin C. Indeed uvidin C was identical with the $NaBH_4$ reduction product (3) of uvidin A (1), and by this way we also established the absolute configuration of uvidin C. The difficulty encountered in the acetylation of the secondary β OH at C-6 could therefore be explained by the severe 1,3-diaxial interaction of the OH with the 10-CH_3 and 4β-CH_3 groups.

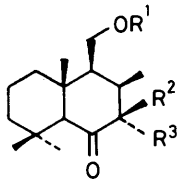
Uvidin D (6), needles from $CHCl_3$, m.p. 152—154 °C, has the same molecular formula $C_{15}H_{26}O_3$ (M^+, 254) as uvidin C.



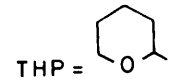
(1) R = H
(2) R = OH



(3) $R^1 = R^2 = H$
(4) $R^1 = Ac, R^2 = H$
(5) $R^1 = R^2 = Ac$



(6) $R^1 = R^3 = H, R^2 = OH$
(7) $R^1 = R^2 = R^3 = H$
(8) $R^1 = R^2 = H, R^3 = OH$
(9) $R^1 = THP, R^2 = R^3 = H$

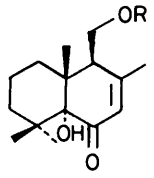


Comparison of its i.r., ^1H n.m.r., and mass spectra with those of (1) suggested that this compound also was a drimane sesquiterpene. The i.r. spectrum showed a ketone absorption (1 715 cm^{-1}) as well as OH absorptions; the mass spectrum showed characteristic fragment ions at *m/z* 151, 123, and 109, also present in the mass spectrum of (1), indicating the position of the ketone at C-6,[6] and precluding the presence of substituents in ring A.[7] However, compound (6) lacked the characteristic features of the epoxy system found in uvidins A (1) and B (2). In the ^1H n.m.r. spectrum of (6), in fact, the signal for 8-CH_3 appeared as a doublet (J 7.2 Hz) at δ 0.81, and that of 7-H again as a doublet (J 7.5 Hz) at δ 4.31, being geminal to a secondary OH group and coupled to 8-H.† From these data the structure of 7-hydroxy-6-oxodrimanol was assigned to compound (6). Moreover the magnitude of coupling constants observed (J 4—7.5 Hz) for the hydrogens at C-7, C-8, and C-9 indicated that these protons are all involved in axial–equatorial interactions, in agreement with the stereochemistry shown in structure (6).

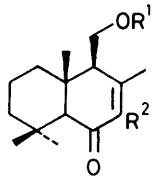
In comparison with the ^1H n.m.r. data of compound (7),[6]

† All ^1H n.m.r. assignments are supported by appropriate decoupling experiments.

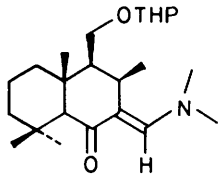
‡ A rather unexpected high-field chemical shift for 5-H was also observed in uvidin C[6] (δ 0.79), in 11-*O*-acetyluvidin C[6] (δ 0.68), and in some new 6β-OH labdane diterpenoids (δ 0.8—0.9) from *Scapania undulata* (J. D. Connolly, presented as plenary lecture at the IXth Conference on Isoprenoids, Prague, September 1981).



(10) R = H
(11) R = Ac



(12) R^1 = H, R^2 = OH
(13) R^1 = R^2 = H
(14) R^1 = Ac, R^2 = H
(15) R^1 = THP, R^2 = OH
(16) R^1 = THP, R^2 = Ac
(17) R^1 = H, R^2 = Ac
(18) R^1 = THP, R^2 = H



(19)

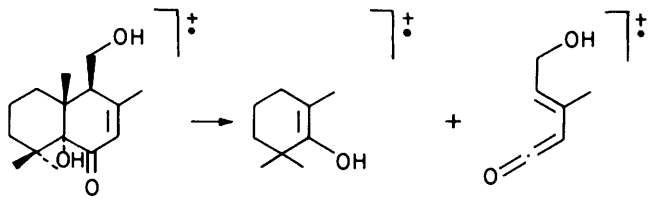
the presence in (6) of an equatorial β-OH group at C-7 caused no appreciable down-field shift for the C-5 and C-9 axial protons, while they *were* shifted, as expected, in the 7α-OH epimer (8). Compound (8) was prepared by hydroxylation of (7) [6] using Vedejs' method: [8] kinetic deprotonation of (7) at C-7 with lithium di-isopropylamide (LDA) gave the corresponding lithium enolate, which was treated at −15 °C with MoO_5–pyridine–HMPA [8] (HMPA = hexamethylphosphoric triamide) to yield the crystalline 7α-hydroxy ketone (8), m.p. 150—152 °C. In agreement with the stereochemistry shown in the formula (8), in the ^{1}H n.m.r. spectrum the C-7 proton showed a vicinal coupling constant of 3.2 Hz, indicative of an equatorial–equatorial interaction with 8-H, and the chemical shifts of 5-H and 9-H moved down-field, relative to the corresponding signals in (7), because of the new 1,3-diaxial interaction with the 7α-OH. Compound (8), when heated at 50 °C in MeOH containing an excess of MeONa, was slowly and only partially converted into another compound, which showed chromatographic properties identical with uvidin D (6). Thus, although sufficiently pure material was not available to allow a direct comparison of spectral data, we believe that compound (8) was partially isomerized, by base, to the desired epimer (6).

Direct chemical correlation of uvidin A (1) with uvidin D (6) through nucleophilic attack on C-8 cannot be contemplated because an unfavourable *trans*-diequatorial opening of the epoxy ring is required.* However, in principle, the β-*cis* configuration of 8-CH_3 and 7-OH in compound (6) could be secured by hydrogenation of the C-7, C-8 double bond of a diosphenol such as compound (12), as the hydrogen uptake should occur from the more accessible α-side of the molecule. Preparation of (12) from (1) was initially tried by the very well known procedure [9] for converting cyclic β-alkyl-α,β-epoxy ketones into α,β-diones with mineral or Lewis acid.

* On the other hand hydrogenolysis of (1) gave 8β-hydroxy-6-oxodrimanol.[6]

In our case, however, treatment of (1) with anhydrous $ZnBr_2$ in benzene, or with dilute aqueous HCl or H_2SO_4, caused extensive rearrangement of the molecule and compound (12) could not be obtained from the reaction mixture. The diosphenol (15) was finally obtained, in 41% overall yield from the tetrahydropyran-2-yl (THP) ether of the known ketone (13) [6] by hydrogenation to (9), followed by conversion into the α-enamino ketone (19) with t-butoxybis(dimethylamino)-methane and then cleavage of the carbon–carbon double bond using singlet oxygen.[10] In the event, however, the C-7,C-8 double bond in (15) and in some derivatives (12), (16), and (17) unexpectedly proved to be extremely resistant to hydrogenation to the corresponding saturated acyloin, either with Pd–C or with PtO_2 in different solvents. This inertness can be explained by the highly hindered tetrasubstituted double bond.

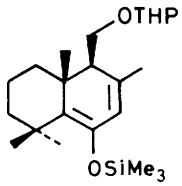
Uvidin E (10) was obtained as fine needles from hexane–diethyl ether, m.p. 127—129 °C, of molecular formula $C_{15}H_{24}O_3$ (M^+, 252), and showed i.r. and u.v. absorptions characteristic of an α,β-unsaturated ketone. In the ^{1}H n.m.r. spectrum the vinylic proton (δ 5.77) showed allylic coupling with a methyl group (δ 2.07) and with the methine of a $CH{-}CH_2OH$ system. Acetylation afforded the monoacetate (11) which still contained a free tertiary OH. Compounds (10) and (11) showed spectral features similar to those of (13), which was obtained [6] by de-epoxidation of uvidin A (1), and to those of the corresponding acetyl derivative (14), but no signal for 5-H was detectable in the ^{1}H n.m.r. spectra. To account for these data the structure of 5α-hydroxy-6-oxodrimenol (10) was assigned to uvidin E. The presence of a tertiary axial OH at C-5 explained the down-field shift of 0.5 p.p.m. for the signal of the 9-H in (10) in comparison with that in (13) and its deshielding effect was markedly accentuated in pyridine solution.[11] Moreover in the mass spectrum of (10) the prominent peaks at *m/z* 140 and 112 could be assigned, as supported by high-resolution mass measurements, to ions (20) and (21) respectively, coming from a retro-Diels–Alder-like fragmentation of uvidin E (10).



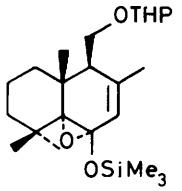
m/z 252 (10) *m/z* 140 (20) *m/z* 112 (21)

The chemical transformation of uvidin A (1) into uvidin E (10) through the key intermediate (13) [6] eventually established the absolute configuration of (10). The required regio- and stereo-selective introduction of an angular α-OH group at C-5 on (13) was achieved by the Rubottom procedure for α-hydroxy ketones.[12] Kinetically controlled deprotonation [13] of the protected enone (18) at the α′ position, *i.e.* at C-5, gave the corresponding enolate which was trapped as its *O*-trimethylsilyl derivative (22).

Crude (22) was treated directly with 1.1 equiv. of *m*-chloroperbenzoic acid to afford the epoxide (23). One could in fact expect that the reaction on the more electron-rich double bond of (22) should occur from the more accessible α face of the molecule, thus leading to the epoxide with the required stereochemistry. By acidic treatment of (23) in a two-phase system we obtained, as expected, the rearrangement of the epoxy alcohol to the acyloin, and the concomitant



(22)



(23)

cleavage of the two protecting groups. Uvidin E (10) was thus obtained, after purification, in 11% overall yield from (13), and was identical (i.r., ^{1}H n.m.r. t.l.c.) with the natural sample isolated as mentioned above.

To our knowledge uvidin E (10) represents the first example of a drimane sesquiterpene with an OH group at C-5. The peculiarity of uvidins seems to be the oxygenated function at C-6 which is present in all the isolated metabolites. As for the biosynthetic pathway of these new uvidins, compounds (3) and (6) may feasibly be derived from uvidin A (1), while for (10) the origin is more intriguing.

Experimental

M.p.s are uncorrected and were determined with a Fisher–Johns hot plate. I.r. spectra were recorded on either Perkin-Elmer 257 or a Perkin-Elmer 197 spectrophotometer, u.v. spectra for solutions in MeOH with a Perkin-Elmer 200 spectrophotometer, and ^{1}H n.m.r. and ^{13}C n.m.r. spectra with a Varian XL-100 or Bruker 80 MHz spectrometer, with tetramethylsilane as internal standard. Electron-impact (e.i.) mass spectra were determined on a Du Pont 21-492 B instrument at 70 eV. High-resolution mass measurements were run on a Finnigan Mat 8230 instrument. Specific optical rotations refer to MeOH solutions and were taken on an automatic Perkin-Elmer polarimeter. Analytical and preparative t.l.c. was carried out by using Merck precoated glass plates (Kieselgel $60F_{254}$) and spots were visualized by spraying with a vanillin–sulphuric acid solution and then heating the plates at 120 °C for 10 min. Column chromatography was performed on Kieselgel 60 Merck (0.040—0.063 mm) or on Woelm DCC silica gel. All reactions were run under an inert atmosphere of N_2 and those requiring anhydrous conditions were performed in oven-dried apparatus. Solvents and reagents were dried according to established procedures by distillation under N_2 from an appropriate drying agent: diethyl ether and tetrahydrofuran (THF) (Na benzophenone ketyl); pentane, hexane, and di-isopropylamine (CaH_2); pyridine (KOH); CH_2Cl_2 (P_2O_5). Dry solvents were stored over molecular sieves under N_2. t-Butoxybis(dimethylamino)methane was purchased from Fluka. Purity of isolated compounds was checked by t.l.c. with at least three different solvent mixtures.

Isolation of Uvidin C (3), *Uvidin D* (6), *and Uvidin E* (10) *from* Lactarius uvidus.—Silica-gel chromatography of a fatty-acid-free extract of *L. uvidus*, using gradient elution with benzene–ethyl acetate, gave several mixtures of drimane sesquiterpenes with intermediate polarity between uvidin A (1) and uvidin B (2).[6] Those with similar chromatographic properties were pooled together to afford eventually five main fractions (A—E). Separation of fraction A (38 mg) by preparative t.l.c. (p.l.c.) [cyclohexane–ethyl acetate (1 : 1)] yielded *uvidin E* (10) (12.7 mg) and uvidin C (3) (5.6 mg). Fraction B (46.3 mg) was chromatographed on dry silica gel (10 g) using gradient elution with cyclohexane–ethyl acetate. Nine fractions (A′—I′) were collected. Fractions E′ and G′ contained pure uvidin C (3) (6.8 mg) and *uvidin D* (6) (7.3 mg) respectively. Rechromatography of fraction F′ (11.4 mg) by p.l.c. [cyclohexane–ethyl acetate (1 : 1)] afforded more *uvidin E* (10) (3 mg).

Uvidin C (3), m.p. 110—112 °C, had i.r., ^{1}H n.m.r., R_F properties identical with those of ' 6-dihydrouvidin A.'[6]

Uvidin D (6) was crystallized from $CHCl_3$, m.p. 152—154 °C (Found: M^+, 254.1887. $C_{15}H_{26}O_3$ requires M, 254.1882); $\nu_{max.}$ (KBr) 3 425, 3 250 (OH), and 1 715 cm^{-1} (CO); δ_H (100 MHz; $CDCl_3$) 0.81 (3 H, d, J 7.2 Hz, 8-CH_3), 0.86 (3 H, s, 10-CH_3), 0.92 (3 H, s, 4β-CH_3), 1.26 (3 H, s, 4α-CH_3), 1.2—1.8 (6 H, m, 1-, 2-, and 3-H_2), 1.97 (1 H, m, 9-H), 2.19 (1 H, s, 5-H), 3.00 (1 H, qdd, $J_{8\text{-}CH_3,8}$ 7.2, $J_{7,8}$ 7.5, $J_{8,9}$ 4.0 Hz, 8-H), 3.72 (1 H, dd, $J_{11,11'}$ 10.5, $J_{11,9}$ 8.5 Hz, 11-H), 3.95 (1 H, dd, $J_{11,11'}$ 10.5, $J_{11',9}$ 5.0 Hz, 11′-H), and 4.31 (1 H, dd, $J_{7,8}$ 7.5, $J_{7,9}$ 1.2 Hz, 7-H); *m/z* 254 (M^+, 13%), 239 (55), 236 (4), 221 (29), 154 (22), 153 (53), 152 (23), 151 (100), 139 (14), 137 (19), 135 (14), 125 (16), 124 (14), 123 (61), 122 (10), 121 (15), 119 (11), 111 (17), 109 (44), 107 (18), 105 (11), 98 (10), 97 (24), 96 (22), 95 (36), 93 (16), 91 (12), 85 (18), 84 (47), 83 (53), 82 (18), 81 (42), 79 (14), 77 (11), 70 (12), 69 (56), 67 (26), 57 (37), 56 (15), 53 (13), 43 (61), and 41 (52).

Uvidin E (10) crystallized as needles from hexane–diethyl ether, m.p. 127—129 °C (Found: M^+, 252.1729. $C_{15}H_{24}O_3$ requires M, 252.1725); $[\alpha]_D^{23}$ +6.4° (*c* 0.4); $\nu_{max.}$ (KBr) 3 370 (OH), and 1 645 and 1 625 cm^{-1} (unsaturated CO); $\lambda_{max.}$ 244.5 nm (log ε 3.95); δ_H (100 MHz; $CDCl_3$) 1.00 (3 H, s, 10-CH_3), 1.19 (3 H, s, 4β-CH_3), 1.27 (3 H, s, 4α-CH_3), 1.4—1.8 (6 H, m, 1-, 2-, and 3-H_2), 2.07 (3 H, t, $J_{8\text{-}CH_3,9} = J_{8\text{-}CH_3,7}$ = 1.3 Hz, 8-CH_3), 2.82 (1 H, m, $J_{11,9}$ 3.5, $J_{11',9}$ 5.5, $J_{9,7}$ 2.7, $J_{8\text{-}CH_3,9}$ 1.3 Hz, 9-H), 3.82 (1 H, dd, $J_{11,11'}$ 11.5, $J_{11',9}$ 5.5 Hz, 11′-H), 3.94 (1 H, dd, $J_{11,11'}$ 11.5, $J_{11,9}$ 3.5 Hz, 11-H), and 5.77 (1 H, m, 7-H); *m/z* 252 (M^+, 7%), 235 (5), 217 (7), 207 (2), 205 (4), 140 (100), 125 (71), 121 (9), 112 (30), 109 (8), 95 (67), 84 (16), 83 (16), 82 (11), 69 (21), 67 (9), 55 (21), 43 (31), and 41 (23). For ion (20) (Found: *m/z* 140.1205. $C_9H_{16}O$ requires *m/z*, 140.1201). For ion (21) (Found: *m/z*, 112.0531. $C_6H_8O_2$ requires *m/z*, 112.0524).

Acetylation of Uvidin C (3) *to Compounds* (4) *and* (5).—Uvidin C (2 mg) was acetylated with Ac_2O–pyridine overnight at room temperature. Recovery of the product in the usual way gave 11-*O*-acetyluvidin C (4), identical (i.r. and ^{1}H n.m.r.) with ' 6-dihydrouvidin A acetate,' obtained[6] by $NaBH_4$ reduction of uvidin A acetate. Compound (4) was redissolved in an excess of stirred Ac_2O–pyridine containing a catalytic amount of 4-dimethylaminopyridine; after 7 h, work-up in the usual way gave 6,11-di-*O*-acetyluvidin C (5) (1.8 mg), $\nu_{max.}$ 1 735 (CO) and 1 240 cm^{-1}; δ_H (80 MHz; $CDCl_3$) 1.00 (3 H, s, 4α-CH_3 or 10-CH_3), 1.12 (6 H, s, 10-CH_3 or 4α-CH_3, and 4β-CH_3), 1.35 (3 H, s, 8-CH_3), 2.10 (3 H, s, CH_3CO), 2.12 (3 H, s, CH_3CO), 3.37 (1 H, d, $J_{6,7}$ 6.0 Hz, 7-H), 4.35 (1 H, dd, $J_{11,11'}$ 13.0, $J_{11,9}$ 6.5 Hz, 11-H), 4.50 (1 H, dd, $J_{11,11'}$ 13.0 Hz, $J_{11',9}$ 4.0 Hz, 11′-H), and 5.52 (1 H, dd, $J_{5,6}$ 5.0, $J_{6,7}$ 6.0 Hz, 6-H).

Synthesis of 7α-*Hydroxy*-6-*oxodrimanol* (8).—A solution of 6-oxodrimanol[6] (7) (27 mg) in THF (3 ml) was added during 3 min by syringe to a solution of LDA (0.272 mmol) in hexane–THF (5 ml) at −78 °C. The solution was stirred for 15 min at −78 °C, then for 10 min at −15 °C, and freshly prepared[8] MoO_5–pyridine–HMPA (80 mg) was added in one portion. This was followed after 2 min by the addition of saturated aqueous $Na_2S_2O_4$ to destroy the excess of reagent. The reaction mixture was then warmed to room temperature, diluted with brine, and extracted with diethyl ether (3 ×).

The combined ethereal extracts were washed with brine, dried ($MgSO_4$), and concentrated under reduced pressure. Dry-column chromatography of the residue over silica gel (3 g) employing $CHCl_3$–MeOH (95 : 2) as eluant gave the acyloin (8) (7 mg) as fine needles, m.p. 150—152 °C; $\nu_{max.}$ (KBr) 3 360 (OH) and 1 698 cm^{-1} (CO); δ_H (100 MHz; $CDCl_3$) 0.88 (3 H, s, 10-CH_3), 0.94 (3 H, s, 4β-CH_3), 0.97 (3 H, d, *J* 7.2 Hz, 8-CH_3), 1.24 (3 H, s, 4α-CH_3), 1.3—1.9 (6 H, m, 1-, 2-, and 3-H_2), 2.27 (1 H, m, 9-H), 2.5 (1 H, m, 8-H), 2.98 (1 H, s, 5-H), 3.65 (1 H, t, $J_{11,11'} = J_{11,9}$ = 10.5 Hz, 11-H), 3.78 (1 H, d, $J_{7,8}$ 3.2 Hz, 7-H), and 3.92 (1 H, dd, $J_{11,11'}$ 10.5, $J_{11',9}$ 5.0 Hz, 11′-H); *m/z* 254 (M^+, 12%), 239 (33), 221 (21), 153 (22), 152 (16), 151 (100), 137 (17), 135 (10), 123 (39), 121 (11), 109 (28), 107 (13), 99 (12), 97 (14), 95 (28), 93 (12), 91 (11), 84 (26), 83 (33), 82 (22), 81 (28), 79 (14), 77 (11), 71 (15), 69 (36), 67 (22), 57 (20), 56 (15), 55 (37), 53 (18), 43 (43), and 41 (45).

Synthesis of 7-*Hydroxy*-6-*oxo*-11-O-*tetrahydropyran*-2-*yldrimenol* (15).—To a solution of 6-oxodrimenol [6] (13) (67 mg) in CH_2Cl_2 (3 ml) was added solid PPTS [14] (71 mg) and dihydropyran (39 μl), then the mixture was stirred at room temperature for 5 h. After dilution with diethyl ether the solution was washed with brine, dried ($MgSO_4$), and concentrated under reduced pressure to give the crude 11-tetrahydropyranyl ether. Purification by chromatography on a silica-gel column [eluant hexane–Me_2CO (4 : 1)] yielded compound (18) as an oil (86 mg), $\nu_{max.}$ 1 670 cm^{-1} (CO); δ_H (80 MHz; $CDCl_3$) 5.85 (1 H, m, 7-H), 4.61 (1 H, br s, OCHO), 4.20—3.30 (4 H, m, 2 × CH_2O), 2.43 (1 H, m, 9-H), 2.11 (1 H, s, 5-H), and 2.02 (3 H, s, 8-CH_3).

Compound (18) (75 mg) in AcOEt (2 ml) was hydrogenated at room temperature and atmospheric pressure in the presence of an excess of Adams catalyst (Fluka), the uptake of hydrogen being very slow (15 h). Work-up as usual gave, after chromatography on a silica-gel column [eluant hexane–Me_2CO (21 : 1)], 6-oxo-11-*O*-tetrahydropyran-2-yldrimanol (9) as an oil (65 mg), $\nu_{max.}$ 1 710 cm^{-1} (CO); δ_H (80 MHz; $CDCl_3$) 0.92 (3 H, d, *J* 7.5 Hz, 8-CH_3).

A solution of compound (9) (40 mg) in t-butoxybis-(dimethylamino)methane (0.5 ml) was stirred and heated at 115 °C for 8 h. A solution of the resulting crude enamino ketone (19) in CH_2Cl_2 (10 ml), through which oxygen gas was gently bubbled, was photo-oxygenated at −78 °C with Rose Bengal (1 mg) as a sensitizer, and a Philips HPK 125-W lamp as a light source using a λ > 500 nm glass filter. After 40 min the irradiation was stopped and the reaction mixture was allowed to warm to room temperature. The solution was concentrated and the residue was separated by column chromatography over silica gel, with hexane–Me_2CO (8 : 1) as eluant, to give 7-hydroxy-6-oxo-11-*O*-tetrahydropyranyldrimenol (15) as an oil (20 mg), $\nu_{max.}$ 3 290 (OH), and 1 673 and 1 648 cm^{-1} (conjugated CO); $\lambda_{max.}$ 272 nm (log ε 3.86); δ_H (80 MHz; $CDCl_3$) 2.08 (3 H, d, $J_{8\text{-}CH_3,9}$ 2.0 Hz, 8-CH_3), 2.25 (1 H, s, 5-H), 2.52 (1 H, m, 9-H), 3.4—4.20 (4 H, m, 2 × CH_2O), 4.65 (1 H, br s, OCHO), and 6.25 (1 H, s, OH).

Acetylation of Uvidin E (10) *to its* 11-O-*Acetate* (11).—Uvidin E (10) (3 mg) was acetylated with Ac_2O–pyridine overnight at room temperature. Recovery of the product as usual and crystallization from hexane gave the acetate (11) as needles, m.p. 148—149 °C, $\nu_{max.}$ (KBr) 3 540 (OH), 1 725 (acetate), and 1 672 and 1 632 cm^{-1} (enone); δ_H (100 MHz; $CDCl_3$) 1.02 (3 H, s, 10-CH_3), 1.22 (3 H, s, 4β-CH_3), 1.29 (3 H, s, 4α-CH_3), 1.4—1.8 (6 H, m, 1-, 2-, and 3-H_2), 1.98 (3 H, t, $J_{8\text{-}CH_3,7} = J_{8\text{-}CH_3,9}$ = 1.5 Hz, 8-CH_3), 2.08 (3 H, s, CH_3CO), 3.06 (1 H, m, 9-H), 4.18 (1 H, dd, $J_{11,11'}$ 12.2, $J_{11,9}$ 6.0 Hz, 11-H), 4.36 (1 H, dd, $J_{11,11'}$ 12.2, $J_{11',9}$ 3.5 Hz, 11′-H), and 5.78 (1 H, m, 7-H); *m/z* 294 (M^+, 7%), 277 (8), 266 (12), 251 (9), 235 (21), 234 (31), 219 (25), 218 (32), 216 (21), 208 (13), 207 (31), 204 (11), 201 (16), 191 (26), 189 (16), 178 (12), 174 (13), 173 (21), 166 (11), 165 (27), 163 (16), 161 (14), 160 (20), 152 (18), 151 (61), 149 (20), 141 (30), 140 (72), 139 (12), 138 (14), 137 (16), 136 (12), 135 (17), 127 (17), 126 (22), 125 (100), 124 (21), 123 (28), 122 (24), 121 (21), 119 (14), 113 (14), 112 (54), 111 (21), 109 (24), 108 (12), 107 (24), 105 (14), 97 (21), 96 (29), 95 (70), 93 (17), 91 (21), 85 (20), 84 (42), 83 (23), 82 (17), 81 (22), 79 (20), 77 (18), 71 (15), 70 (14), 69 (52), 68 (14), 67 (27), 65 (13), 57 (21), 56 (17), 55 (53), 53 (21), 43 (97), and 41 (83).

Synthesis of Uvidin E (10).—A solution of compound (18) (26 mg) in THF (1 ml) was added dropwise to a stirred solution of LDA (0.11 mmol) in hexane–THF (1 : 2) (1.2 ml) at −78 °C. The reaction was stirred at −78 °C for 30 min, and the temperature was allowed to rise to −10 °C (during 30 min). Trimethylchlorosilane (20 μl) was added and the solution was stirred for 2 h at room temperature, then evaporated to dryness under reduced pressure. The residue was redissolved in pentane and the mixture was filtered to remove the inorganic salts. After evaporation of pentane, a solution of the crude silyl derivative (22) in hexane (0.8 ml) was added to a solution of *m*-chloroperbenzoic acid (17 mg) in hexane (0.8 ml) at −15 °C. After being stirred for 1 h at room temperature, the reaction mixture was filtered and the hexane was removed under reduced pressure. Then, the residue was partitioned between diethyl ether (1 ml) and 1M HCl (1 ml). After 4 h at room temperature, solid $NaHCO_3$ was added, followed by diethyl ether (5 ml) and the aqueous phase was separated. Drying ($MgSO_4$) and removal of solvent under reduced pressure afforded crude compound (10). Purification by p.l.c. [eluant cyclohexane–ethyl acetate (1 : 1)] gave uvidin E (2.5 mg) which was identical (t.l.c., i.r., ^1H n.m.r.) with a natural sample.

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