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SYNTHETIC STUDIES ON BIOLOGICALLY ACTIVE NATURAL COMPOUNDS. PART II: CORRELATION OF CINNAMODIAL WITH UVIDIN A AND STEREOSPECIFIC TRANSFORMATION INTO (-)-PERENIPORIN A.

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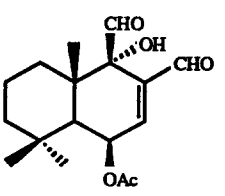
Abstract. The selective reduction of the aldehyde groups of (-)-cinnamodial (**1**) was investigated. In this way a partial synthesis of (-)-pereniporin A (**2**) was achieved, as well as that of the triol **3**, previously obtained from (+)-uvidin A (**4**).[1]

Introduction. In the preceding paper of this series[1] we described the stereospecific transformation of (+)-uvidin A (**4**)[2] into the triol **3**, which then was selectively oxidized to (-)-cinnamodial (**1**),[3] a drimane sesquiterpene with remarkable insect antifeedant activity. In order to get a sample of the triol **3** for a direct comparison with the synthetic material, and for studying its conversion back to cinnamodial, the reduction of the dialdehyde **1** was thoroughly investigated. Our efforts culminated in an efficient partial synthesis of compound **3** and in a clean transformation of (-)-cinnamodial (**1**) into natural (-)-pereniporin A (**2**), a drimane sesquiterpene isolated from liquid cultures of Perenniporia medullaepanis (Basidiomycetes).[4] Pereniporin A shows cytotoxicity against Friend leukemia cells, F5-5, as well as antimicrobial activity against a strain of Bacillus subtilis and plant growth regulation property.[4] No synthesis, even partial, of compound **2** has been accomplished so far. Moreover, the absolute configuration was assigned as **2** to pereniporin A merely for biosynthetic reasons;[4] neither chemical nor spectral evidences



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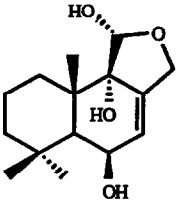

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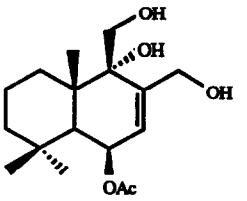

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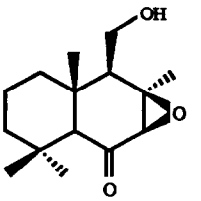

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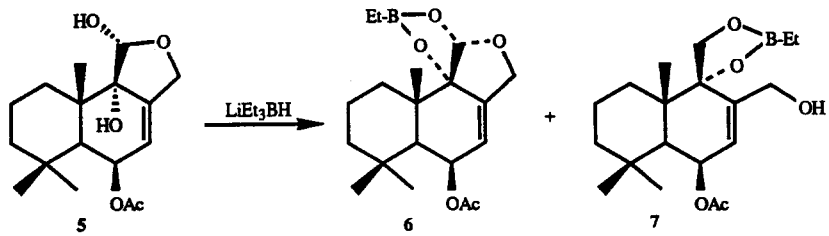
have been given so far to corroborate this stereochemical assignment.

Results and discussion

At the onset of our project we hoped that contemporaneous reduction of the two carbonyl groups of compound **1** to the corresponding hydroxy moieties at C-11 and C-12 might be feasible. However, the first results using borohydride reductants were discouraging.[5] For example reduction with $NaBH_4$ (with or without added $CeCl_3$) in MeOH or EtOH, $LiBH_4$ or KBH_4 in THF, Bu_4NBH_4 in AcOEt, gave a mixture of products or led to a decomposition of the starting material **1**. With Al hydrides reduction of **1** proceeded only partially, affording, however, a well characterized product. As a matter of fact the hemiacetal **5** was obtained in 83 % yield by reduction of **1** with $LiAlH(\underline{t}\text{-BuO})_3$ in THF or, less efficiently, with $LiAlH_4$ or DIBAL in THF at 0°C. Two remarkable features of this reaction are the complete chemo- and site-selectivity of the hydride attack and the inactivity of the hemiacetal **5** to further reduction, even with an excess of $LiAlH_4$.



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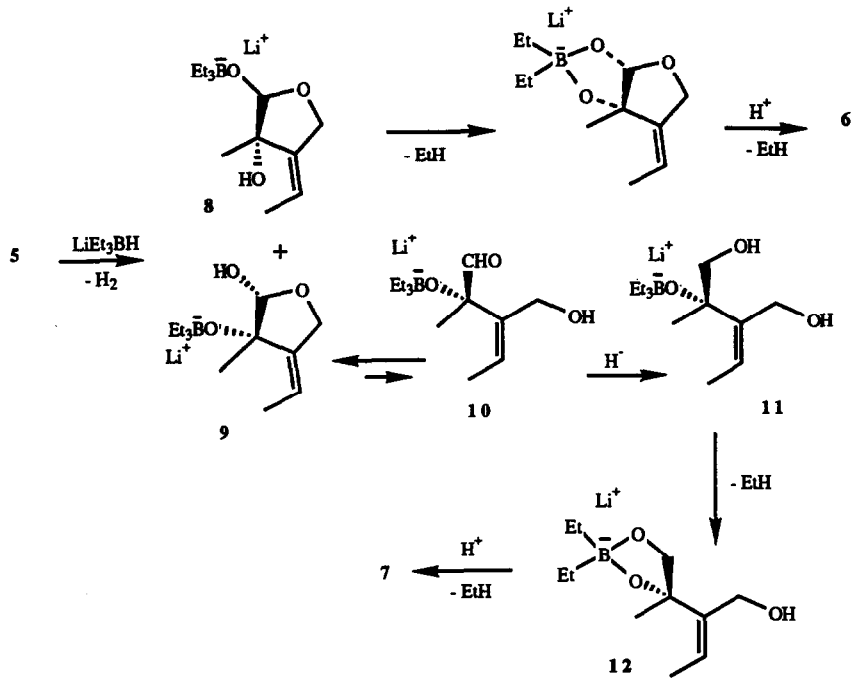
It was anticipated that the more exposed and more electrophilic α,β-unsaturated aldehyde group at C-12 of **1** would react faster than the OH-bonded formyl group at C-11; however, the sluggishness of the 6-OAc group towards the usual ester reductants was rather unexpected. Evidently the formation of the highly congested sp^3 intermediate upon attack of the hydride on the acetate group, is severely hindered by the two axially protruding methyl groups at C-4 and C-10. In addition, the ^{1}H-NMR spectrum (300 MHz) of compound **5** showed that no appreciable amounts of either the epimeric acetal at C-11 or the tautomeric free hydroxy-aldehyde species were present. Thus the carbonyl group at C-11 is sheltered from hydride attack as, in the above reduction conditions, it cannot be efficiently unmasked by cleavage of the strong intramolecular H-bonding of the hemiacetal with the 9α-OH group. The *cis* stereochemistry of the 1,2-diol system in **5** was established on the basis of the results of the reaction of compound **5** with $LiEt_3BH$, which afforded a mixture (6:1) of the two ethylboronates **6** and **7** in 80% overall yield. Direct reduction of cinnamodial (**1**) with $LiEt_3BH$ proceeds through the initial formation of the hemiacetal **5**, giving then the same

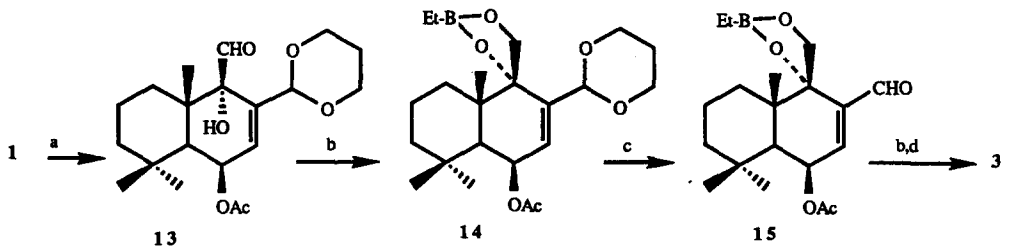


Scheme I

mixture of compounds **6** and **7**. Later on this behaviour of syn 1,2-diols towards lithium trialkylborohydrides was shown to be general, leading to a new method of preparing alkylboronates.[6] The possibility of reducing the protected carbonyl function of **5** with Super-Hydride®, unlike with other hydride reagents, seems to depend on the initial formation of the ate complexes **8** and **9** (scheme I), according to the mechanism proposed by us.[6] The complex **8** can evolve only into the boronate **6**, whereas the less favoured salt **9**, formed with the sterically more demanding tertiary OH group, may have another option, if the hemiacetal group at C-11 is no more involved in a strong intramolecular H-bond. In such a case an equilibrium can in fact be installed between the species **9** and the hydroxy-aldehyde **10**, thus leaving the carbonyl group unprotected towards further reduction to the alcohol **11**. The latter is rapidly transformed into **7** as a result of the preferential formation of the five membered boron complex **12** over the isomeric six membered ring involving the allylic OH group at C-12. Interestingly the acetate group at C-6 could not be reduced even with $LiEt_3BH$. The structures of the boronates **6** and **7** were supported by the spectroscopic data and by further chemical transformations. Deprotection of **7** with 30% H_2O_2 in aq MeOH gave the triol **3** in quantitative yield. Exposure of **6** to 30% H_2O_2 in aq NaOH afforded

pereniporin A (2) in 90% yield. The spectral and physical data of this product, including the optical rotation, were in full agreement with those reported in the literature for the natural compound.[4] Thus pereniporin A has the same absolute configuration of cinnamodial (1)[3] and uvidin A (4).[2]

As the contemporaneous reduction of the two aldehyde groups of cinnamodial (1) proved to be disappointingly impracticable, we decided to protect, as acetal, the less hindered and more reactive unsaturated formyl group, before reducing the other one. Although this transformation appeared straightforward, in practice, exposure of cinnamodial (1) to 1,3-propandiol and cat. p-TsOH, slowly afforded the monoprotected acetal **13** in very modest yield (40%). Moreover, compound **13** was decomposed with alcoholic $NaBH_4$. Therefore, once more, we resorted to the use of $LiEt_3BH$, as it was anticipated that the hydroxy group resulting from reduction of the aldehyde **13** could be trapped in the cyclic boronate **14**. Such a protection would have allowed the unmasking of the formyl group at C-12 in acidic



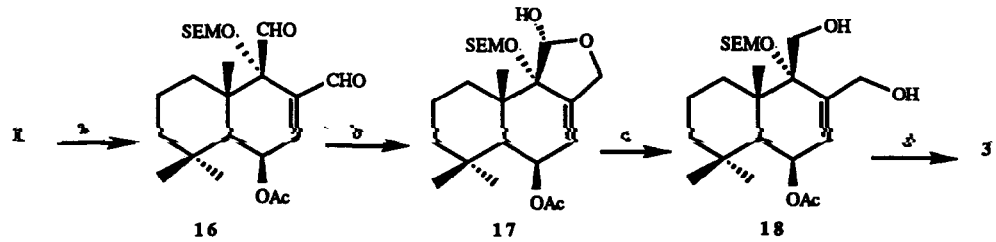
a, HO~~OH, p-TsOH; b, $LiEt_3BH$; c, aq HCl; d, 30% H_2O_2, MeOH

Scheme II

conditions and its easy reduction to the corresponding allylic alcohol, without any complication arising from a hemiacetal formation. Actually the reactions of scheme II were performed according to our expectations giving the triol **3** in a satisfactory 66% overall yield from **13**.

In a continued effort to prepare the triol **3** from cinnamodial (1) more efficiently, we decided to protect the labile angular hydroxy-group in 1 as the β-(trimethylsilyl)-ethoxymethyl ether, using SEM-Cl and $i\text{-Pr}_2NEt$[7] to give **16** in 70% yield.

Contrary to the previous experiments with cinnamodial (1), now the reduction of the protected derivative **16** proceeded smoothly with Bu_4NBH_4 in AcOEt, affording the diol **18** as the only isolable product (scheme III). Even better yield (75%) of compound **18** could be obtained by carrying out the reduction in two steps, using first $LiAlH(t\text{-BuO})_3$ to give **17**, and then Bu_4NBH_4 to reduce the hemiacetal group slowly, but clearly.



a, SEM-Cl, i-Pr_2NEt, CH_2Cl_2; b, LiAlH(t-BuO)$_3$, THF; c, Bu_4NBH_4, AcOEt; d, 48% HF, CH_3CN

Scheme III

Finally, exposure of **18** to HF in CH_3CN effected clean deprotection of the tertiary OH group giving the triol **3** in 84% yield. This product was identical in all respects with the compound previously prepared from uvidin A (**4**) and converted into cinnamodial (**1**).[1] Thus this route represents an indirect chemical correlation between cinnamodial (**1**) and uvidin A (**4**).

EXPERIMENTAL

Melting points were determined on a Fisher–Johns hot-stage apparatus and are uncorrected. I.r. spectra were recorded as neat oils or as KBr pellets or nujol dispersions for solids on a Perkin-Elmer 197 spectrometer. Mass spectra were obtained on a Finnigan MAT 8222 instrument at 70 eV (0.5 mA). ^{1}H NMR spectra were recorded on a Bruker WP80 SY or a Bruker CPX300 instruments in $CDCl_3$, except otherwise stated. Chemical shifts are reported in δ units with Me_4Si as the internal standard; the abbreviations s=singlet, d=doublet, t=triplet, q=quartet, m=multiplet, and b=broad are used throughout. Optical rotations were determined in a $CHCl_3$ solution, except otherwise indicated, with a digital Perkin-Elmer 241 polarimeter. Column chromatography was performed on Kieselgel 60 (Merck), 0.04–0.06 mm, slurry packed, and run at atmospheric pressure. Analytical TLC plates (250 μm) were obtained from Merck. All solvents were purified and dried by standard techniques just before use. All reactions were routinely carried out under an inert atmosphere of dry nitrogen. All organic solutions were washed with brine, then dried over $MgSO_4$ and filtered prior to rotary evaporation at water aspirator pressure. Residual solvent was removed under vacuum, usually at less than 1 torr.

6-O-Acetylpereniporin A (**5**) Solid LiAlH(t-BuO)$_3$ (31 mg, 0.12 mmol) was added to a stirred solution of cinnamodial (**1**) (25 mg, 0.081 mmol) in dry THF (2 mL), at room temperature. After 25 min., the reaction was quenched with aq NH_4Cl and the mixture was extracted with $CHCl_3$ (3x8 mL). Drying and removal of solvent gave a residue which was chromatographed (hexane–AcOEt, 60:30) to yield **5** (21 mg, 83%) as a pasty solid, $[\alpha]_D^{20}$ - 216.97° (*c* 0.4); ν_{max} 3450, 3010, 2980, 2940, 2870, 1740, 1465, 1375, 1250, 1080, 1050, 1030, 950, 940, 915, 850 cm^{-1}; δ (300 MHz) 0.99, 1.15 and 1.17 (3H each, 3s, 4-$(CH_3)_2$ and 10-CH_3), 2.03 (1H, d, $J_{5,6}$ = 4.8 Hz, 5-H), 2.06 (3H, s, CH_2COO-), 4.23 (1H, dt, J_{AB}=13.5 Hz, J_{12b-7}=J_{12b-6} = 1.6 Hz, 12-Ha), 4.89 (1H, dt, J_{AB} = 13.5 Hz, J_{12b-7} = J_{12b-6} = 2.3 Hz, 12-Hb), 5.36 (1H, brs, 11-H), 5.61 (1H, m, 6-H), 5.68 (1H, m, 7-H); m/z (%) 280 (M-CH_2O, 1), 279 (M-CH_2OH),

149(31), 147(32), 144(27), 137(28), 135(52), 134(35), 126(100), 123(40), 121(47), 119(26), 109(82), 107(27), 105(36), 97(28), 95(35), 91(36), 81(30), 69(53), 55(21), 43(22).

Ethylboronates **6** and **7**. 135 μL of 1M $LiEt_3BH$ in THF was added to a stirred solution of cinnamodial (**1**) (19 mg, 0.061 mmol) in anhydrous THF (1.5 mL), at -10°C. After 5 min, Et_2O (15 mL) was added, and the reaction was quenched with two drops of 10% HCl, at -10°C. The mixture was washed with 5% $NaHCO_3$, brine, and dried. After drying and removal of solvent, the residue was chromatographed (hexane-AcOEt, 3:1) to yield, in order of elution, the ethylboronates **6** (13 mg, 61%) and **7** (2.5 mg, 12%). The same procedure was followed for the reaction of **5** (9 mg, 0.029 mmol) with 40 μL of 1M $LiEt_3BH$ in THF, giving a mixture (6:1) of **6** and **7** in 80% overall yield. Compound **6**, m.p. 72-74°C, ν_{max} 2939, 1732, 1463, 1360, 1320, 1274, 1239, 1178, 1131, 1094, 1062, 1013, 948, 919, 860, 825, 760 cm^{-1}; δ (80 MHz) 0.98 (3H, br t, CH_3-CH_2B), 1.02, 1.15 and 1.17 (3H each, 3s, 4-$(CH_3)_2$ and 10-CH_3), 2.08 (3H, s, CH_3COO), 4.38 (2H, br s, collapsed ABq, 12-Ha and 12-Hb), 5.50-5.87 (3H, m, 11-H, 6-H and 7-H); m/z (%) 348 (M, 7), 319(20), 306(98), 288(11), 277(10), 259(45), 233(100), 217(25), 204(22), 189(32), 187(15), 161(12), 149(13), 123(17), 109(26), 105(12), 95(12), 91(12), 83(12), 81(11), 69(26), 55(23), 43(82), 41(24). Compound **7**, δ (80 MHz) 0.95 (3H, br t, CH_3CH_2B), 1.05, 1.10 and 1.16 (3H each, 3s, 4-$(CH_3)_2$ and 10-CH_3), 2.00 (1H, d, J_{5-6} = 4.8 Hz, 5-H), 2.08 (3H, s, CH_3COO), 4.00-4.50 (4H, m, 11-H and 12-H), 5.68 (1H, t, $J_{5-6} = J_{6-7} \simeq$ 5.0 Hz, 6-H), 6.05 (1H, d, J_{6-7} = 5.0 Hz, 7-H); m/z (%) 350 (M, 0.3), 308 (7.5) 290 (7.5), 226 (46), 189(10), 184(52), 166(100), 165(28), 110(20), 109(15), 105(13), 95(10), 91(11), 81(13), 69(26), 57(10), 55(22), 43(68), 41(27).

Triol **3** by hydrolysis of ethylboronate **7**. 30% H_2O_2 (60 μL) was added to a solution of boronate **7** (2.5 mg, 7.10^{-3} mmol) in MeOH (1 mL) containing 300 μL H_2O. After 10 min at room temperature the reaction was quenched with aq Na_2SO_3 and the mixture diluted with $CHCl_3$ (6 mL). The organic layer was washed with brine, dried and taken to dryness. The residue (mg 2.1, 96%) was identical in all respects with the triol **3**[1] by direct comparison.

(-)-Pereniporin A (**2**). A solution of ethylboronate **6** (12 mg, 0.034 mmol) in MeOH (1.5 mL), containing aq 10% NaOH (300 μL), was heated at 50°C for 40 min. Then, to the mixture cooled to 0°C, were added in the order, 30% H_2O_2 (300 μL) and, after 10 min, 10% H_2SO_4 to neutrality. The mixture was taken up in CH_2Cl_2 (12 mL) and washed with aq Na_2SO_3, then with brine. After drying and removal of solvent, the residue was chromatographed (hexane-AcOEt, 50:50) to give compound **2** (8.3 mg, 90%), m.p. 157-160°C (lit.[4] 164-166°C), $[\alpha]_D^{20}$ -184° (MeOH, c 0.2) (lit.[4] -181°); ν_{max} 3496, 3399, 3004, 2943, 2925, 2865, 1462, 1423, 1387, 1363, 1312, 1292, 1224, 1205, 1126, 1088, 1047, 1026, 1005, 940, 908, 883, 860, 840, 769 cm^{-1}; δ (CD_3OD) 1.08, 1.15 and 1.34 (3H each, 3s, 4-$(CH_3)_2$ and 10-CH_3), 1.83 (1H, d, J_{5-6}=5.0 Hz, 5-H), 1.92 (1H, br t, 1-H), 4.17 (1H, br d, J_{AB} = 12.5 Hz, 12-Ha), 4.46 (1H, m, 6-H), 4.54 (1H, dt, J_{AB} = 12.5 Hz, J" = 2.0 Hz, 12-Hb), 5.33 (1H, s, 11-H), 5.65 (1H, m, 7-H); m/z (%) 250 (M-H_2O, 15), 235(17), 232(33), 222(21), 217(21), 207(29), 204(22), 203(23), 189(42), 175(16), 161(47), 153(31), 151(27), 149(35), 147(82), 145(17), 144(35), 137(40), 135(27), 133(20), 126(100), 123(22), 119(25), 109(35), 105(26), 97(34), 95(19), 91(24), 83(24), 81(22), 71(21), 69(38), 55(31), 43(24), 41(28).
These data are in agreement with those reported for (-)-pereniporin A (**2**).[4]

Monoprotection of cinnamodial (**1**) with 1,3-propandiol: acetal **13**. Excess 1,3-propandiol (40 equiv) and a catalytic amount of p-TsOH were added to a stirred solution of cinnamodial (**1**) (20 mg, 0.065 mmol) in dry benzene (1 mL), at room temperature. After 5 h, Et_2O (10 mL) was added, and the organic layer was washed with 5% $NaHCO_3$ and brine. After drying and removal of solvent, the residue was chromatographed (hexane-AcOEt, 80:20) to give the acetal **13** (9.5 mg, 40%), m.p. 186-190°C, ν_{max} 3473, 2978, 2929, 2910, 2870, 2850, 1726, 1708, 1461,

1370, 1346, 1310, 1296, 1280, 1248, 1214, 1152, 1125, 1098, 1048, 1029, 1014, 950, 918, 898, 880, 862, 848, 805, 785 cm^{-1}; δ (80 MHz) 1.00, 1.15 and 1.42 (3H each, 3s, 4-$(CH_3)_2$ and 10-CH_3), 2.00 (1H, d, J_{5-6} = 5.0 Hz, 5-H), 2.08 (3H, s, CH_3COO), 3.50-4.37 (4H, m, $OCH_2CH_2CH_2O$-) 4.92 (1H, s, 12-H), 5.70 (1H, t, $J_{5-6} = J_{6-7}$ = 5.0 Hz, 6-H), 6.40 (1H, d, J_{6-7} = 5.0 Hz, 7-H), 9.90 (1H, s, 11-H); m/z(%) 366 (M, 0.2), 338(21), 337(75), 307(18), 306(65), 295(46), 279(22), 278(66), 277(100), 249(24), 237(23), 221(20), 219(43), 203(19), 201(37), 196(15), 195(13), 191(12), 183(17), 182(67), 177(17), 175(13), 173(16), 171(30), 163(22), 161(16), 151(15), 149(31), 141(21), 137(17), 135(18), 133(17), 125(11), 123(27), 121(24), 114(11), 111(11), 110(37), 108(18), 105(25), 101(63), 95(22), 93(14), 91(14), 87(66), 83(20), 81(22), 79(11), 77(15), 69(39), 67(13), 59(27), 55(37), 43(86), 41(54).

Ethylboronate **14**. To a magnetically stirred solution of acetal **13** (12 mg, 0.033 mmol) in dry THF (1.5 mL) was added by syringe at 0°C a 1.0 M solution of $LiEt_3BH$ in THF (70 μL). After the reaction mixture was stirred for 5 min, it was quenched with AcOEt (0.5 mL), and then poured into saturated aq NH_4Cl. The aq layer was extracted with CH_2Cl_2 (3x8 mL), which was dried and concentrated in vacuo. The residue (11.5 mg), consisting of **14** practically pure, was used in the following step; ν_{max} 2960, 2880, 1735, 1465, 1410, 1370, 1305, 1280, 1245, 1208, 1150, 1125, 1110, 1095, 1050, 1025, 1010, 950, 920, 855, 840, 795, 770, 755 cm^{-1}; δ (80 MHz) 0.90 (3H, brt, J=6.0 Hz, CH_3CH_2B), 0.97, 1.05 and 1.10 (3H each, 3s, 4-$(CH_3)_2$ and 10-CH_3), 2.00 (1H, d, J_{5-6} = 5.0 Hz, 5-H), 2.04 (3H, s, CH_3COO-), 3.50-4.35 (4H, m, $-OCH_2CH_2CH_2$-), 4.07 (1H, d, J_{AB} = 10 Hz, 11-Ha) 4.47 (1H, d, J_{AB} = 10 Hz, 11-Hb), 5.02 (1H, s, 12-H), 5.70 (1H, t, $J_{5-6} = J_{6-7}$ = 5.0 Hz, 6-H), 6.30 (1H, d, J_{6-7} = 5.0 Hz, 7-H); m/z(%) 406 (M, 5), 364(15), 346(15), 282(100), 281(60), 241(28), 240(95), 239(55), 164(83), 110(22), 101(65), 87(86), 81(18), 69(32), 59(26), 57(20), 55(28), 43(71), 41(35).

Hydrolysis of acetal **14**, followed by reduction with $LiEt_3BH$ to give the triol **3**. To a magnetically stirred solution of compound **14** (11 mg, 0.027 mmol) in THF (1.0 mL) was added 2.5% aq HCl (300 μL). After the reaction mixture was stirred for 6 h at room temperature, it was taken up in Et_2O (12 mL), washed with 5% $NaHCO_3$, and dried. After removal of solvent under vacuum the residue, corresponding to the aldehyde **15** [M =348 (MS); δ_H = 9.5 (1H, s, CHO, 12-H), 6.82 (1H, d, J = 5 Hz, 7-H)], was immediately used in the following step. Therefore, to a solution of **15** (8.5 mg, 0.024 mmol) in dry THF (1 ml) was added at 0°C a 1.0 M solution of $LiEt_3BH$ in THF (31 μL), followed, after 10 min, in the order, by 100 μL of MeOH and 80 μL of 30% H_2O_2. The reaction mixture was taken up in CH_2Cl_2 and the organic layer was washed with 5% aq Na_2SO_3, then with brine. Drying and removal of solvent gave a residue which was chromatographed (hexane-AcOEt, 1:2) to afford the triol **3** (6.5 mg, 77% from **14**), $[\alpha]_D^{20}$ - 139.3° (c 0.3), identical with the compound previously prepared from uvidin A (**4**).

9-O-ß-(Trimethylsilyl)ethoxymethyl ether of cinnamodial: **16**. To a magnetically stirred solution of cinnamodial (**1**) (14 mg, 0.045 mmol) in dry CH_2Cl_2 (1 mL) was added by syringe i-Pr_2NEt (45 μL) and ß-(trimethylsilyl)ethoxymethyl chloride (SEM-Cl) (22.6 mg, 0.136 mmol). After stirring the reaction mixture for 6 h at 35-40°C, more i-Pr_2NEt (45 μL) and SEM-Cl (22.6 mg) were added, and stirring was continued for 20 more hours at 35°C. Then volatiles were evaporated under vacuum and the yellow residue was chromatographed (hexane-AcOEt, 10:1) to afford 13.9 mg (70%) of **16** as an oil; ν_{max} (cm^{-1}) 2930, 2860, 1735, 1690, 1460, 1365, 1230, 1205, 1165, 1100, 1015, 930, 855, 830, 750; δ (80 MHz) 0.02 (9H, s, $(CH_3)_3Si$). 0.62-1.00 (2H, m, $Si-CH_2-CH_2$-), 1.02, 1.17 and 1.23 (3H each, 3s, 4-$(CH_3)_2$ and 10-CH_3), 2.15 (3H, s, CH_3COO). 2.22 (1H, d, J_{5-6} = 5.0 Hz, 5-H), 3.25-3.65 (2H, m, $Si-CH_2-CH_2-O$), 4.27 (2H, collapsed ABq, $O-CH_2-O$), 5.90 (1H, t, $J_{5-6} = J_{6-7}$ = 5.0 Hz, 6-H), 6.90 (1H, d, J_{6-7} = 5.0 Hz, 7-H), 9.50 (1H, s, 12-H), 9.66 (1H, s, 11-H); ECNI (isobutane) m/z 438 (M), 437, 378, 348.

9-O-ß-(Trimethylsilyl)ethoxymethyl ether of 6-O-acetylpereniporin A: **17**. $LiAlH(t\text{-}BuO)_3$ (25 mg, 0.098 mmol) was added to a stirred solution of protected cinnamodial **16** (23.5 mg, 0.053 mmol) in dry THF (1.5 mL), at room temperature. After 15 min the mixture was diluted with Et_2O and the reaction was quenched with saturated aq NH_4Cl. Drying and removal of solvent gave a residue which was chromatographed (hexane-AcOEt, 8:1) to afford 19.5 mg (83%) of **17** as a glassy oil; ν_{max} 3450, 2945, 2915, 2860, 1735, 1465, 1420, 1390, 1370, 1245, 1222, 1195, 1165, 1145, 1100, 1050, 1020, 1010, 945, 915, 885, 858, 835, 750, 730, 690 cm^{-1}; δ (80 MHz) 0.04 (9H, s, $(CH_3)_3$ Si), 0.82.-1.12 (2H, m, Si-$\underline{CH_2}$-CH_2), 1.01 (3H, s, CH_3) 1.18 (6H, s, $2CH_3$) , 2.00 (1H, d, J_{5-6} = 5.0 Hz, 5-H), 2.10 (3H, s, CH_3COO), 3.55-3.90 (2H, m, $SiCH_2\underline{CH_2}O$), 4.25 (1H, brd, J_{AB}=14 Hz, 12-Ha), 4.55 (1H, br d, J_{AB}=14 Hz, 12-Hb), 4.75 (2H, collapsed ABq, OCH_2O), 5.30 (1H, s, 11-H), 5.62 (1H, m, 6-H), 5.85 (1H, m, 7-H); ECNI (isobutane) m/z 440 (M), 378, 294, 234, 219, 205.

9-O-ß-(Trimethylsilyl)ethoxymethyl ether of triol **3** : **18**. Solid Bu_4NBH_4 (9 mg, 0.035 mmol) was added to a stirred solution of the hemiacetal **17** (13 mg, 0.029 mmol) in dry AcOEt (1.2 mL), at room temperature. After 36 h the reaction mixture was diluted with Et_2O (10 mL), washed with saturated aq NH_4Cl, and dried. Removal of solvent gave a residue which was chromatographed (hexane-AcOEt, 2:1) to afford 11.5 mg (90%) of **18** as a sticky oil; ν_{max} 3446, 2927, 2871, 1735, 1462, 1370, 1246, 1054, 1023, 938, 860, 836, 757 cm^{-1}; δ (80 MHz) 0.02 (9H, s, $(CH_3)_3$ Si), 0.81-1.05 (2H, m, Si-$\underline{CH_2}$-CH_2), 0.93 (3H, s, CH_3), 1.10 (6H, s, $2CH_3$), 1.92 (1H, d, J_{5-6}=5.0 Hz, 5-H), 2.04 (3H, s, CH_3COO), 3.42-3.90 (2H, m, $SiCH_2\underline{CH_2}O$), 3.85 (2H, br s, collapsed ABq, 11-H), 4.18 (2H, br s, collapsed ABq, 12-H), 4.68 (2H, ABq, OCH_2O), 5.54 (1H, t, $J_{5-6} \simeq J_{6-7}$ = 4.5 Hz, 6-H), 6.05 (1H, d, J_{6-7} = 4.5 Hz, 7-H); ECNI (isobutane) m/z 442 (M), 292, 248.

Deprotection of the SEM ether **18** to give the triol **3**. To a magnetically stirred solution of the diol **18** (10 mg, 0.023 mmole) in CH_3CN (1.5 mL) was added 48% aq HF (100 µL) at 0°C. After 45 min, the reaction mixture was diluted with $CHCl_3$ (8 mL), washed with 5% aq $NaHCO_3$, and dried. Removal of solvent gave a residue which was chromatographed (hexane-AcOEt, 30:60) to afford 6 mg (84%) of the triol **3**, identical in all respects with a sample prepared from uvidin A/4 [1].

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