Chemistry of zamoranic acid. Part 10.† Homochiral hemisynthesis of pereniporin A

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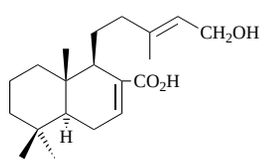
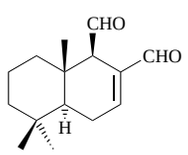
The synthetic versatility of 12-acetoxydrima-7,9(11)-diene 1 obtained from 15-hydroxylabda-7,13-dien-17-oic acid (zamoranic acid), as a key intermediate in the homochiral semisynthesis of highly functionalized drimanes such as pereniporin A 3, an important antibiotic, through the carbonate 2, is highlighted.

Introduction

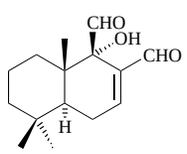
The drimanes are sesquiterpenes that exhibit a wide range of biological activities.[1] Due to the importance of these properties, much work has been carried out on their synthesis and semisynthesis, using in the latter case a large number of natural products.[2] For several years we have been studying the transformation of zamoranic acid into active drimanes.[3] Zamoranic acid belongs to the labdane class of sesquiterpenes and was isolated as the major component from *Halimium viscosum*.[4] It is an ideal precursor[5] for antifeedant drimanes such as polygodial, isolated from *Polygonum hydropiper*,[6] warburganal, isolated from *Warburgia ugandensis*,[7] or antibiotic drimanes such as pereniporin A and B, isolated from the filtered culture of the basidiomycete *Perenniporia medullaepanis*.[8] Pereniporin A exhibits antimicrobial activity against *Bacillus subtilis*, it inhibits the root elongation of lettuce and shows cytotoxicity against Friend leukaemia cells at 130 μg ml^{-1}.



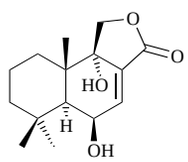
Zamoranic acid



Polygodial



Warburganal

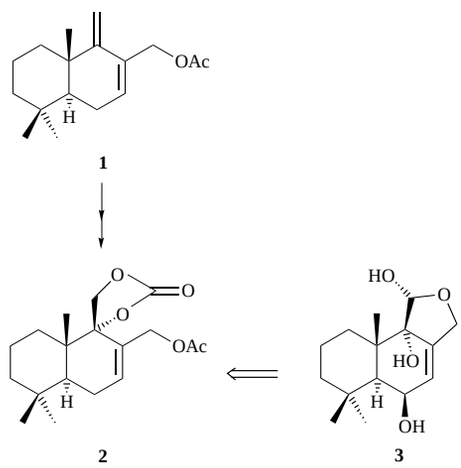


Pereniporin B

Results and discussion

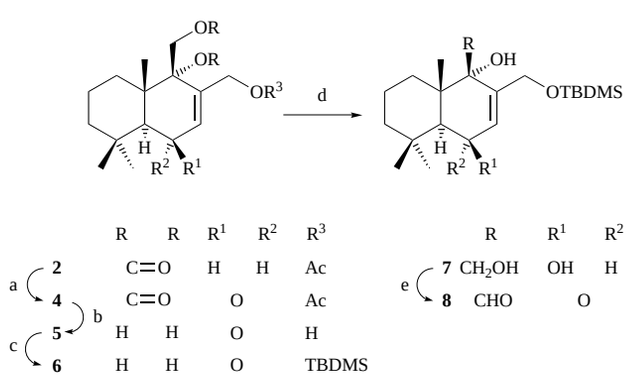
Recently we reported the preparation of carbonate **2** from diene **1**, which was obtained from 15-hydroxylabda-7,13-dien-17-oic acid (zamoranic acid).[3] It was thought that allylic oxidation at C-6 of compound **2**, carbonate ring-opening and oxidation at C-11 would lead to an aldehyde that after deprotection of the hydroxy group at C-12 and cyclization would give pereniporin A, **3** (Scheme 1).

The treatment of **2** with CrO_3–HOAc[9] gave the required ketone **4** in an acceptable yield (52%). This ketone was hydrolysed to the triol **5** that was selectively protected with *tert*-butyldimethylsilyl chloride (TBDMSCl) to give the compound



Scheme 1

6. Reduction of the ketone to the required β-hydroxy compound **7** was achieved with DIBAL-H. Any attempt to selectively oxidize C-11 to an aldehyde failed, giving in all cases **8** (Scheme 2).

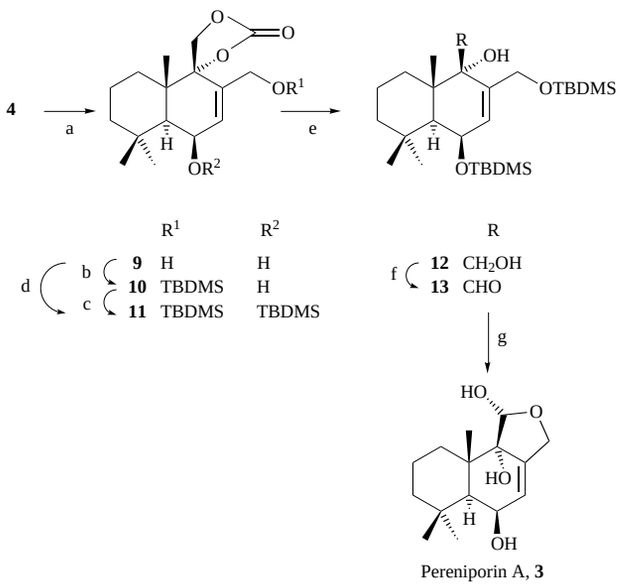


Scheme 2 *Reagents and conditions:* a, CrO_3, HOAc, 52%; b, 5% K_2CO_3 in MeOH, 80%; c, TBDMSCl, DMAP, imidazole, DMF, 77%; d, DIBAL-H, CH_2Cl_2, −78 °C, 95%; e, Swern, 34%

Because of these results, a new route from **4** was designed. The selective deprotection of C-12 with retention of the carbonate protecting group was achieved *via* reduction with four equivalents of $NaBH_4$ in THF–MeOH at 40 °C. Under these conditions diol **9** was obtained (Scheme 2). The reaction of **9** under the usual conditions with TBDMSCl gave only monoprotected product **10**. It was necessary to use TBDMSOTf[10] to obtain compound **11**. The selective hydrolysis of the carbonate rather than the silyl groups was carefully undertaken, the best conditions being 2 M NaOH in dioxane, to give diol **12**, a com-

† For Part 9 in the series, see ref. 3.

pound previously reported by Mori and Takaishi.[11] After Swern oxidation of **12** to obtain aldehyde **13**, both silyl groups were removed using TBAF, and the resulting triol cyclized to afford pereniporin A, **3** (Scheme 3). The IR and ^{1}H NMR spectra of



Scheme 3 *Reagents and conditions:* a, $NaBH_4$, $CeCl_3$, MeOH–THF, 40 °C, 82%; b, TBDMSCl, DMAP, imidazole, DMF, 90%; c, TBDMS-OTf, 2,6-lutidine, CH_2Cl_2, 0 °C, 95%; d, c, 90%; e, 2 M NaOH, 1,4-dioxane, 79%; f, Swern, 93%; g, 1.1 M TBAF in THF, 74%

the synthetic material were identical with those of natural pereniporin A.[8a]

This semisynthesis of (−)-pereniporin A in eleven steps from zamoranic acid, in 4.0% overall yield, demonstrates the synthetic utility of diene **1**.

Experimental

General details

Unless otherwise stated, all chemicals were purchased as the highest purity commercially available and were used without further purification. Melting points were determined with a Kofler hot stage melting point apparatus and are uncorrected. IR spectra were recorded on a BOMEM 100 FT IR spectrophotometer. ^{1}H and ^{13}C NMR spectra were performed in deuteriochloroform and referenced to the residual peak of $CHCl_3$ at δ 7.26 and δ 77.0, for ^{1}H and ^{13}C respectively, in a Bruker WP-200 SY spectrometer. Chemical shifts are reported in δ(ppm) and coupling constants (J) are given in Hz. Mass spectra and accurate mass measurements were recorded on an AEI MS-902 or a VG Micromass 7070E spectrometer. Microanalysis was carried out using a Perkin-Elmer 2400 CHN Elemental Analyser. Optical Rotations were determined in a Perkin-Elmer 241 polarimeter in 1 dm cells and are given in units of 10^{-1} deg cm^2 g^{-1}. Diethyl ether, THF and benzene were distilled from sodium, and pyridine and dichloromethane were distilled from calcium hydride under an Ar atmosphere. Ether refers to diethyl ether.

Allylic oxidation of 12-acetoxy-9α,11-carbonyldioxydrim-7-ene 2: 12-acetoxy-9α,11-carbonyldioxydrim-7-en-6-one 4

To a stirred solution of **2** (24 mg, 0.07 mmol) in acetic acid (0.7 ml) was added CrO_3 (70 mg, 0.7 mmol) at room temperature and the mixture was stirred for 15 h, then it was diluted with water (20 ml) and extracted with ether (3 × 20 ml). The combined organic phases were washed with 5% aqueous $Na_2S_2O_3$, saturated aqueous $NaHCO_3$ and brine, dried, filtered and evaporated. The residue was chromatographed (SiO_2, *n*-hexane–EtOAc 4:1) yielding 13 mg (52%) of **4**, mp 129–130 °C (Found: C, 64.27; H, 7.2. $C_{18}H_{24}O_6$ requires C, 64.27; H, 7.2%); $[\alpha]_D^{21}$ −62.1 ($CHCl_3$, *c* 1.56); ν_{max}(film)/cm^{-1} 1805, 1745, 1682, 1380, 1222, 1126, 1065; δ_H 6.15 (1H, s, H-7), 4.87 (1H, d, *J* 14.0, H_A-12), 4.78 (1H, d, *J* 14.0, H_B-12), 4.48 (2H, s, H-11), 2.73 (1H, s, H-5), 2.13 (3H, s, OCOCH_3), 1.18, 1.17, 0.97 (3 × 3H, 3 × s, Me-15, Me-14, Me-13, respectively); δ_C see Table 1; *m*/*z* 336 ([M]$^+$, 6%), 294 (3), 276 (83), 232 (5), 212 (36), 170 (100), 149 (31), 126 (100), 109 (75), 91 (56), 69 (78) [Found: (EI) M$^+$, 336.1572. $C_{18}H_{24}O_6$ requires *M*, 336.1573].

Hydrolysis of 4: 9α,11,12-trihydroxydrim-7-en-6-one 5

A solution of 3% K_2CO_3 in MeOH (0.47 ml) was added to compound **4** (11 mg, 0.033 mmol). The reaction mixture was stirred at room temperature for 15 min, then water was added and the mixture extracted with EtOAc, washed with 2 M HCl and water, dried with Na_2SO_4, filtered and evaporated. The crude reaction product was chromatographed (SiO_2, *n*-hexane–EtOAc 1:2) affording 7 mg (80%) of **5** (Found: C, 67.15; H, 9.00. $C_{15}H_{24}O_4$ requires C, 67.14; H, 9.01%); $[\alpha]_D^{20}$ −62.4 (CH_3OH, *c* 0.94); ν_{max}(film)/cm^{-1} 3380, 1660, 1212, 1030, 870; δ_H($CDCl_3$) 5.88 (1H, s, H-7), 4.50 (1H, d, *J* 13.8, H_A-12), 4.30 (1H, d, *J* 13.8, H_B-12), 3.87 (2H, s, H-11), 2.89 (1H, s, H-5),

Table 1 ^{13}C NMR data, δ(ppm) in $CDCl_3$

C	4	5[a]	6	7	9[a]	10	11	12	13
1	30.5	32.6	31.5	32.5	32.3	31.4	31.5	32.4	33.5
2	17.2	29.0	18.0	18.7	19.1	18.0	17.9	18.5	18.1
3	42.1	43.8	42.5	44.2	45.4	43.9	44.1	44.2	44.3
4	32.5	33.2	32.3	34.2	35.1	34.2	33.9	33.8	34.1
5	58.9	57.2	56.2	46.4	*b*	46.7	47.3	46.9	46.5
6	197.6	203.3	200.8	65.6	64.7	64.8	65.3	65.5	65.7
7	133.5	126.1	128.4	130.9	136.3	133.8	134.0	131.0	130.7
8	143.3	161.1	153.6	139.0	134.4	134.0	132.8	137.9	135.8
9	85.5	75.9	74.9	75.2	88.9	86.9	87.2	75.0	81.4
10	44.3	46.7	44.7	40.4	40.8	39.6	39.6	40.2	41.6
11	62.8	61.8	62.1	62.7	64.1	64.2	63.8	62.6	204.9
12	66.2	62.6	65.0	66.9	68.0	66.4	66.4	67.0	64.6
13	33.0	34.3	33.7	33.0	32.6	32.2	32.0	32.7	32.8
14	21.4	22.3	21.9	25.2	25.0	25.0	24.5	24.7	24.7
15	17.9	18.6	17.9	19.1	17.9	18.0	17.6	18.7	20.6
–OCOO–	153.7				151.6	152.4	154.8		
Bu^t*C*Si			18.2	18.3		18.5	18.2 (2)	18.1 (2)	18.3, 18.2
Bu^{t}CSi			25.8	25.9		25.9	26.1, 25.9	26.0, 25.7	26.1, 25.9
Me_2Si			−5.0, −5.2	−5.3, −5.0		−5.4, −5.3	−5.5 (2), −3.6 (2)	−5.0 (2), −3.9, −3.1	−5.5 (2), −3.7, −3.3
CH_3COO	170.1								
CH_3COO	20.5								

[a] In CD_3OD. [b] Not observed.

1.19, 1.15, 0.94 (3 × 3H, 3 × s, Me-15, Me-14, Me-13, respectively); δ_H(CD_3OD) 6.01 (1H, s, H-7), 4.41 (2H, s, H-12), 3.71 (2H, s, H-11), 2.90 (1H, s, H-5), 1.17, 1.11, 1.02 (3 × 3H, 3 × s, Me-15, Me-14, Me-13, respectively); δ_C see Table 1; *m*/*z* 268 ([M]$^+$, 3%), 250 (11), 237 (34), 220 (12), 207 (6), 189 (11), 163 (11), 144 (37), 126 (83), 109 (61), 97 (39), 81 (53), 69 (100) [Found: (EI) M$^+$, 268.1676. $C_{15}H_{24}O_4$ requires *M*, 268.1675].

Selective protection of 5: 12-*tert*-butyldimethylsilyloxy-9α,11-dihydroxydrim-7-en-6-one 6

To a solution of the triol **5** (33 mg, 0.12 mmol) in DMF (0.05 ml), catalytic 4-(*N*,*N*-dimethylamino)pyridine and imidazole (34 mg, 0.50 mmol) at room temperature under argon was added *tert*-butyldimethylsilyl chloride (23 mg, 0.15 mmol) and the resulting mixture was stirred for 22 h at room temperature. Then it was diluted with water, extracted with CH_2Cl_2, dried, evaporated and chromatographed (SiO_2, *n*-hexane–EtOAc 19:1) affording 36 mg (77%) of protected alcohol **6** (Found: C, 65.96; H, 9.95. $C_{21}H_{38}O_4Si$ requires C, 65.92; H, 10.01%); ν_{max}(film)/cm^{-1} 3440, 1660, 1460, 1255, 1095, 965, 840; δ_H 5.85 (1H, s, H-7), 4.46 (1H, d, *J* 13.0, H_A-12), 4.36 (1H, d, *J* 13.0, H_B-12), 3.90–3.60 (3H, m, 2H-11, -O*H*), 2.84 (1H, s, H-5), 1.21, 1.16, 0.98 (3 × 3H, 3 × s, Me-15, Me-14, Me-13, respectively), 0.93 (9H, s, Bu^t), 0.14, 0.13 (2 × 3H, 2 × s, Me_2Si); δ_C see Table 1; *m*/*z* 382 ([M]$^+$, 2%), 351 (11), 307 (14), 277 (17), 256 (8), 233 (7), 203 (24), 183 (35), 109 (43), 91 (29), 75 (100) [Found: (EI) M$^+$, 382.2540. $C_{21}H_{38}O_4Si$ requires *M*, 382.2539].

Reduction of 6 with DIBAL-H: 12-*tert*-butyldimethylsilyloxydrim-7-ene-6β,9α,11-triol 7 and 12-*tert*-butyldimethylsilyloxydrim-7-ene-6α,9α,11-triol, C-6 epimer of 7

DIBAL-H (1.5 M in toluene; 0.16 ml, 0.24 mmol) was added to a solution of **6** (21 mg, 0.055 mmol) in dry CH_2Cl_2 (1 ml) at −78 °C under argon and the reaction mixture was stirred for 20 min at −78 °C. Water (0.01 ml, 0.55 mmol) was added and the reaction mixture was warmed to room temperature then dried with Na_2SO_4, filtered and evaporated to give, after chromatography (SiO_2, *n*-hexane–EtOAc 9:1), 20 mg (95%) of **7** and 1 mg (5%) of the C-6 epimer of **7**.

Compound 7. (Found: C, 65.60; H, 10.52. $C_{21}H_{40}O_4Si$ requires C, 65.58; H, 10.48%); ν_{max}(film)/cm^{-1} 3440, 1460, 1250, 1045, 940, 828; δ_H 5.86 (1H, d, *J* 5.2, H-7), 4.46 (1H, dd, *J* 5.2, 4.4, H-6), 4.35 (1H, d, *J* 12.7, H_A-12), 4.27 (1H, d, *J* 12.7, H_B-12), 3.82 (1H, d, *J* 10.7, H_A-11), 3.63 (1H, d, *J* 10.7, H_B-11), 1.73 (1H, d, *J* 4.4, H-5), 1.33, 1.12, 1.07 (3 × 3H, 3 × s, Me-15, Me-14, Me-13, respectively), 0.91 (9H, s, Bu^t), 0.12 (6H, s, Me_2Si); δ_C see Table 1; *m*/*z* 386 ([M$^+$ + 2], 14%), 368 (11), 353 (31), 341 (15), 323 (9), 309 (13), 284 (63), 256 (100), 242 (23), 149 (15), 109 (21), 95 (28), 81 (53), 69 (100), 55 (100).

C-6 Epimer of compound 7. (Found: C, 65.57; H, 10.50. $C_{21}H_{40}O_4Si$ requires C, 65.58; H, 10.48%); ν_{max}(film)/ cm^{-1} 3340, 1470, 1250, 1215, 1055, 1005, 960, 835; δ_H 5.73 (1H, s, H-7), 4.37 (1H, d, *J* 12.0, H_A-12), 4.22 (1H, m, H-6), 4.19 (1H, d, *J* 12.0, H_B-12), 3.94 (1H, br s, OH), 3.8–3.6 (2H, m, H-11), 3.48 (1H, br s, OH), 1.70 (1H, d, *J* 10.3, H-5), 1.26, 1.18, 1.10 (3 × 3H, 3 × s, Me-15, Me-14, Me-13, respectively), 0.91 (9H, s, Bu^t), 0.13, 0.11 (2 × 3H, s, 2 × Me_2Si); *m*/*z* 386 ([M$^+$ + 2], 1%), 353 (32), 291 (16), 261 (10), 235 (15), 187 (47), 161 (18), 105 (52), 75 (100), 69 (59), 55 (59).

Swern oxidation of 7: 12-*tert*-butyldimethylsilyloxy-9α-hydroxy-6-oxodrim-7-en-11-al 8

Oxalyl chloride (3.5 μl, 0.04 mmol) in CH_2Cl_2 (0.1 ml) was cooled to −60 °C. A solution of DMSO (6 μl, 0.08 mmol) in CH_2Cl_2 (0.1 ml) was slowly added over a 5 min period. A solution of **7** (15 mg, 0.039 mmol) in CH_2Cl_2 (0.2 ml) was added dropwise and stirred for 50 min at −60 °C. Triethylamine (27 μl, 0.19 mmol) was added and the reaction kept at −60 °C for 5 min, warmed to room temperature and then quenched with water, extracted with ether and washed successively with 0.5 M HCl, 5% aqueous $NaHCO_3$ and water, dried (Na_2SO_4), filtered and evaporated yielding, after chromatography (SiO_2, *n*-hexane–EtOAc 19:1), 5 mg (34%) of **8** (Found: C, 66.27; H, 9.52. $C_{21}H_{36}O_4Si$ requires C, 66.27; H, 9.58%); ν_{max}(film)/cm^{-1} 3380, 1710, 1666, 1460, 1250, 1060, 835; δ_H 9.92 (1H, s, H-11), 5.96 (1H, s, H-7), 4.20 (2H, s, H-12), 2.83 (1H, s, H-5), 1.29, 1.21, 1.16 (3 × 3H, 3 × s, Me-15, Me-14, Me-13, respectively), 0.89 (9H, s, Bu^t), 0.06 (6H, s, Me_2Si).

Reduction of 4: 9α,11-carbonyldioxydrim-7-ene-6β,12-diol 9

To a solution of **4** (100 mg, 0.30 mmol) and $CeCl_3$ (150 mg, 0.61 mmol) in methanol (3 ml) and THF (3 ml) was added $NaBH_4$ (11 mg, 0.29 mmol) and the mixture warmed to 40 °C and stirred for 20 h, diluted with saturated aqueous NH_4Cl (15 ml) and extracted with ether, washed with brine, dried (Na_2SO_4), filtered and evaporated. The residue was chromatographed (SiO_2, *n*-hexane–EtOAc 1:2) yielding 72 mg (82%) of **9** (Found: C, 64.88; H, 8.22. $C_{16}H_{24}O_5$ requires C, 64.84; H, 8.16%); $[\alpha]_D^{21}$ −134.9 (CH_3OH, *c* 0.86); ν_{max}(film)/cm^{-1} 3380, 1740, 1260, 1068, 1008, 925; δ_H(CD_3OD) 5.99 (1H, d, *J* 5.5, H-7), 4.64 (1H, d, *J* 9.5, H_A-12), 4.40 (1H, m, H-6), 4.36 (1H, d, *J* 9.5, H_B-12), 4.14 (1H, d, *J* 12.0, H_A-11), 4.02 (1H, d, *J* 12.0, H_B-11), 1.20 (3H, s), 0.97 (6H, s); δ_C see Table 1.

Protection of 9: 12-*tert*-butyldimethylsilyloxy-9α,11-carbonyldioxydrim-7-en-6β-ol 10

To a solution of **9** (72 mg, 0.24 mmol) in DMF (50 μl), catalytic 4-(*N*,*N*-dimethylamino)pyridine and imidazole (66 mg, 0.97 mmol) at room temperature under argon was added *tert*-butyldimethylsilyl chloride (91 mg, 0.61 mmol) and the resulting mixture stirred for 1 day at room temperature. Then it was diluted with water, extracted with CH_2Cl_2, dried, evaporated and chromatographed (SiO_2, *n*-hexane–EtOAc 4:1) affording 90 mg (90%) of protected alcohol **10** (Found: C, 64.40; H, 9.30. $C_{22}H_{38}O_5Si$ requires C, 64.35; H, 9.33%); $[\alpha]_D^{20}$ −79.2 ($CHCl_3$, *c* 0.36); ν_{max}(film)/cm^{-1} 3500, 1785, 1460, 1380, 1246, 1135, 1060, 835; δ_H 6.08 (1H, d, *J* 4.0, H-7), 4.77 (1H, d, *J* 9.0, H_A-12), 4.56 (1H, m, H-6), 4.33 (1H, d, *J* 9.0, H_B-12), 4.23 (2H, s, H-11), 1.30 (3H, s), 1.09 (6H, s), 0.90 (9H, s, Bu^t), 0.10, 0.09 (2 × 3H, 2 × s, Me_2Si); δ_C see Table 1.

Protection of 9: 6β,12-bis(*tert*-butyldimethylsilyloxy)-9α,11-carbonyldioxydrim-7-ene 11

To a solution of **9** (17 mg, 0.057 mmol) in CH_2Cl_2 (0.26 ml) and 2,6-lutidine (2,6-dimethylpyridine) (29 μl, 0.25 mmol) at 0 °C under argon was added *tert*-butyldimethylsilyl trifluoromethanesulfonate (52 μl, 0.228 mmol) and the resulting mixture stirred for 15 h at room temperature. Then it was diluted with water, extracted with CH_2Cl_2, dried, evaporated and chromatographed (SiO_2, *n*-hexane–EtOAc 19:1) affording 27 mg (90%) of diprotected alcohol **11** (Found: C, 64.00; H, 10.52. $C_{28}H_{52}O_5Si_2$ requires C, 64.07; H, 9.99%); $[\alpha]_D^{22}$ −116.3 ($CHCl_3$, *c* 1.24); ν_{max}(film)/cm^{-1} 1810, 1470, 1260, 1232, 1115, 960, 840; δ_H 6.04 (1H, d, *J* 4.7, H-7), 4.70 (1H, d, *J* 9.5, H_A-12), 4.54 (1H, m, H-6), 4.32 (1H, d, *J* 9.5, H_B-12), 4.23 (1H, d, *J* 12.0, H_A-11), 4.13 (1H, d, *J* 12.0, H_B-11), 1.24, 1.10, 1.03 (3 × 3H, 3 × s, Me-15, Me-14, Me-13, respectively), 0.90, 0.88 (2 × 9H, 2 × s, Bu^t), 0.14 (6H, s, Me_2Si), 0.09 (6H, s, Me_2Si); δ_C see Table 1.

Hydrolysis of 11: 6β,12-bis(*tert*-butyldimethylsilyloxy)drim-7-ene-9α,11-diol 12

Aqueous 2 M NaOH (0.22 ml) was added to **11** (12 mg, 0.023 mmol) in 1,4-dioxane (0.41 ml) and stirred at room temperature for 2 h. The reaction mixture was extracted with ether, washed with 2 M HCl and water. The combined organic layers were dried (Na_2SO_4), filtered and evaporated. The residue was chromatographed (SiO_2, *n*-hexane–EtOAc 49:1) affording 4 mg (33%) of starting material **11** and 6 mg (79% of the transformed **11**) of **12**. $[\alpha]_D^{22}$ −102.3 ($CHCl_3$, *c* 0.6) (Found: C, 65.40; H, 10.43. $C_{27}H_{54}O_4Si_2$ requires C, 65.00; H, 10.91%); ν_{max}(film)/cm^{-1}

3480–3200, 1460, 1250, 1110, 1075, 970, 840; δ_H 5.73 (1H, d, *J* 5.2, H-7), 4.46 (1H, t, *J* 5, H-6), 4.35 (1H, d, *J* 12.0, H_A-12), 4.17 (1H, d, *J* 12.0, H_B-12), 3.80–3.60 (2H, m, H-11), 3.40 (1H, s, -OH), 1.23, 1.09, 0.99 (3 × 3H, 3 × s, Me-15, Me-14, Me-13, respectively), 0.89, 0.86 (2 × 9H, 2 × s, Bu^t), 0.10 (12H, s, 2 × Me_2Si); δ_C see Table 1.

Swern oxidation of 12: 6β,12-bis(*tert*-butyldimethylsilyloxy)-9α-hydroxydrim-7-en-11-al 13

Oxalyl chloride (3 μl, 0.04 mmol) in CH_2Cl_2 (0.2 ml) was cooled at −60 °C. A solution of DMSO (6 μl, 0.08 mmol) in CH_2Cl_2 (0.2 ml) was slowly added over a 5 min period. A solution of **12** (6.5 mg, 0.013 mmol) in CH_2Cl_2 (0.4 ml) was added dropwise and the mixture stirred for 1 h at −60 °C. Triethylamine (18 μl, 0.13 mmol) was added and the reaction kept at −60 °C for 5 min, warmed to room temperature and quenched with water and extracted with ether. The combined extracts were washed successively with 0.5 M HCl, 5% aqueous $NaHCO_3$ and water, dried, filtered and evaporated yielding, after chromatography (SiO_2, *n*-hexane–EtOAc 49:1), 6 mg (93%) of **13** (Found: C, 65.28; H, 10.53. $C_{27}H_{52}O_4Si_2$ requires C, 65.27; H, 10.55%); ν_{max}(film)/cm^{-1} 3460, 1715, 1460, 1255, 1070, 955, 835; δ_H 9.86 (1H, s, H-11), 5.91 (1H, d, *J* 5.2, H-7), 4.51 (1H, m, H-6), 4.06 (1H, d, *J* 11.7, H_A-12), 3.96 (1H, d, *J* 11.7, H_B-12), 1.42, 1.24, 1.00 (3 × 3H, 3 × s, Me-15, Me-14, Me-13, respectively), 0.89, 0.86 (2 × 9H, 2 × s, Bu^t), 0.13 (6H, s, Me_2Si), 0.02 (3H, s, MeSi), 0.01 (3H, s, MeSi); δ_C see Table 1.

Deprotection of 13: pereniporin A 3

Dry tetra-*n*-butylammonium fluoride (1.1 M solution in THF; 0.35 ml, 0.39 mmol) was added to **13** (6 mg, 0.012 mmol) at room temperature and the mixture was stirred for 4 h at 50 °C and then for 1 day at room temperature. The mixture was poured into water (1 ml) and extracted with ethyl acetate. The organic layers were combined and washed with brine, dried over Na_2SO_4, filtered and evaporated under reduced pressure. The residue was chromatographed (SiO_2, *n*-hexane–EtOAc 7:3) affording 2.4 mg (74%) of **3**, $[\alpha]_D^{22}$ −170.5 (MeOH, *c* 0.24); ν_{max}(film)/cm^{-1} 3450, 3430, 3390, 2980, 2940, 2900, 1465, 1425, 1390, 1365, 1130, 1090, 1050, 1030, 1010, 915, 865; δ_H(CD_3OD) 5.69 (1H, ddd, *J* 4.0, 2.0, 1.5, H-7), 5.35 (1H, s, H-11), 4.58 (1H, dt, *J* 12.5, 2.0, H_A-12), 4.50 (1H, m, H-6), 4.21 (1H, dt, *J* 12.5, 1.5, H_B-12), 1.39, 1.19, 1.13 (3 × 3H, 3 × s, Me-15, Me-14, Me-13, respectively).

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