New Synthetic Routes to Spiroacetals. The 3,4-Dihydro-2*H*-pyran Approach to (±)-Talaromycin B

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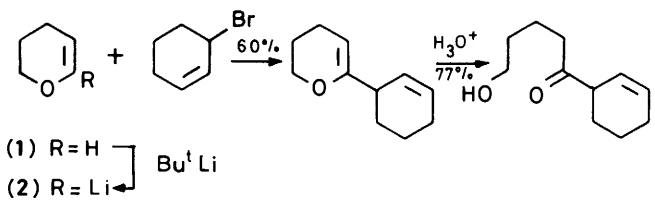
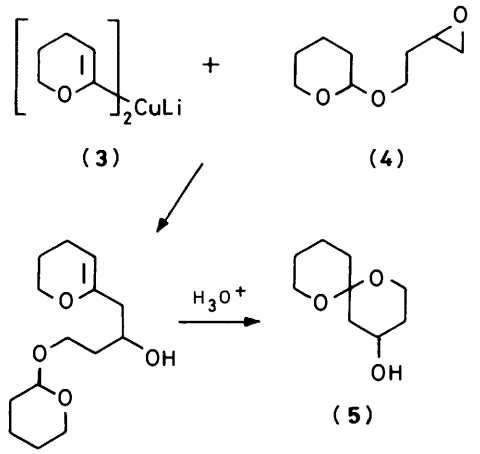
The nucleophilic cleavage of the oxirane (**9**) by the organocuprate derived from 3-ethyl-6-lithio-3,4-dihydro-2*H*-pyran (**7**) was the key step in a synthesis of racemic talaromycin B (**12**). A similar synthesis of desethyltalaromycin B (**15**) from (**9**) and 6-lithio-3,4-dihydro-2*H*-pyran was achieved.

In 1977 Boeckman and Bruza[1] showed that a wide variety of 3,4-dihydro-2*H*-pyrans could be cleanly metallated with Bu^{t}Li in tetrahydrofuran (THF) at 0 °C. Like their acyclic counterparts such as α-methoxyvinyl-lithium,[2,3] these cyclic vinyl ether carbanions behaved as typical strongly basic hard nucleophiles undergoing nucleophilic addition to carbonyls and nucleophilic substitution on primary iodides and allylic bromides. Since the resultant enol ethers were highly susceptible to hydrolysis, the 6-lithio-3,4-dihydro-2*H*-pyrans served as masked bifunctional acyl anion equivalents of 5-hydroxypentanal as illustrated in Scheme 1.[1]



Scheme 1.

We recently reported an approach to 4-hydroxy-1,7-dioxaspiro[5.5]undecane (**5**)[4] (Scheme 2) which exploited the



Scheme 2.

nucleophilicity of the anion (**2**) and the susceptibility of the enol ether function to intramolecular electrophilic addition of a suitably placed side chain hydroxy function to construct the spiroacetal.[5,6] Central to the success of this approach was the nucleophilic scission of the unreactive monosubstituted oxirane (**4**). Precedent suggested that α-alkoxyvinyl-lithiums react only sluggishly — if at all — with oxiranes.[1,3] Fortunately, the relatively stable organocuprate (**3**)[7] derived from reaction of (**2**) with CuI gave a clean and fast reaction with oxirane (**4**) and subsequent aqueous acidic work-up afforded the olive fly pheromone (**5**).[4] We now report full details[8] of a strategically similar synthesis of racemic talaromycin B (**12**).

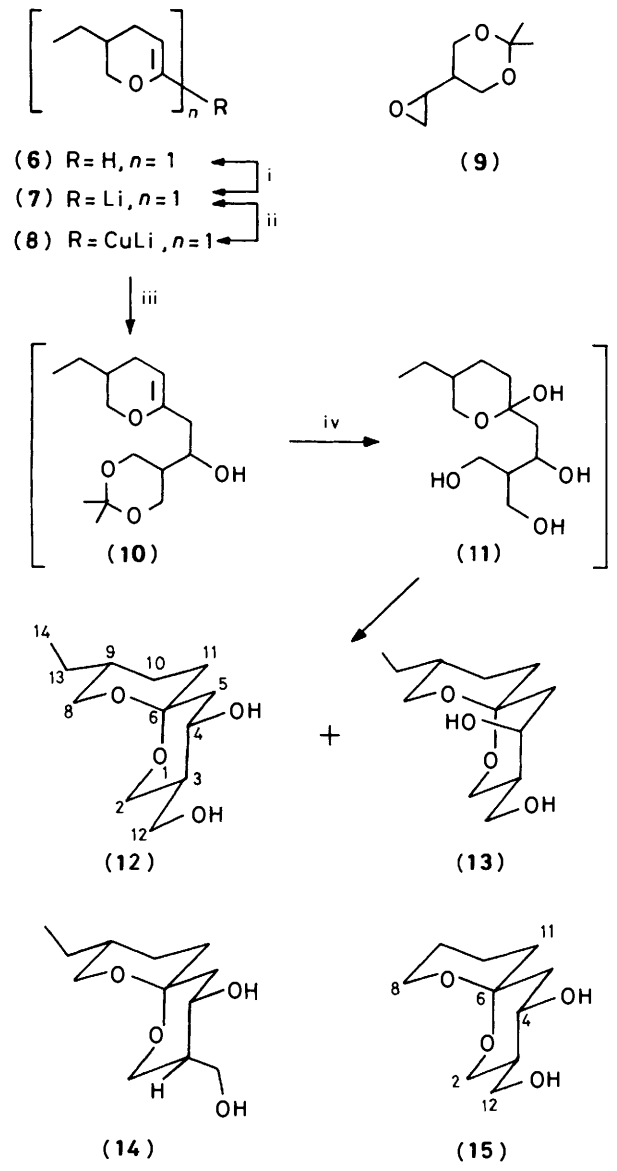
Talaromycins A (**14**) and B (**12**) are isomeric toxic metabolites produced by the fungus *Talaromyces stipitatus* which infects chicken feedstock.[9] Several syntheses of (**12**) have appeared,[9-12] including one which establishes the absolute configuration.[13] The closing stages of our synthesis (Scheme 3) begins with the union of fragments (**6**) and (**9**) *via* the black, heterogeneous organocuprate (**8**). Without purification, the intermediate (**10**) was hydrolysed *via* (**11**) to give a mixture of products from which pure talaromycin B and the isomer (**13**) were isolated in 23% and 14% yield respectively after column chromatography. By a similar sequence, desethyltalaromycin B (**15**) was prepared from (**3**) and (**9**) in 49% overall yield.

The structure of the products was assigned from their 400 MHz ^{1}H and 22.5 MHz ^{13}C n.m.r. spectroscopic data given in Tables 1 and 2 respectively. The ^{1}H n.m.r. spectrum of (**12**) was in excellent agreement with the 360 MHz data for natural talaromycin B published by Lynn and co-workers.[9] Furthermore, both isomers (**12**) and (**13**) gave virtually identical fragmentation patterns on electron impact mass spectroscopy which included the fragments (**16**)—(**19**) characteristic of spiroacetals.[14]

The key dihydropyran (**6**) was prepared in six steps from the readily available aldehyde (**20**)[15] in 36% overall yield as shown in Scheme 4. The conversion of the aldehyde (**20**) into the lactone (**22**) could not be achieved efficiently by $NaBH_4$ reduction followed by lactonization. However, large scale catalytic hydrogenation over PtO_2 in the presence of $SnCl_2$ as a promoter[16] gave rapid and efficient reduction of the aldehyde function in (**20**) to the carbinol (**21**) provided the catalyst was intermittently revived by introducing small amounts of oxygen. The lactonization of (**21**) and subsequent steps were routine.

The conversion of the phenyl selenoether (**24**) into the olefin (**28**) (Scheme 5) was the weakest link in the chain of 5 steps by which the oxirane (**9**) was synthesized in 26% overall yield from commercial diethyl cyclopropane-1,1-dicarboxylate (**23**). A variety of conditions were examined for the conversion (**26**)⟶(**28**)[17] but the yield could not be made to exceed 30—36% at best. Although the yield of terminal olefin (**28**) from the *o*-nitrophenyl selenoether (**27**)[18] was improved to 60%, the route used to prepare (**27**) was too long to compete favourably with the sequence shown in Scheme 5.

A major blemish in the synthesis described above results from the use of the racemic precursors (**6**) and (**9**). The consequent lack of diastereoisomeric control between the remote chiral centres at C-4 and C-9 in (**12**) leads to a statistical 1:1 mixture of (**12**) and (**13**) in the first instance which is not reflected in the product composition because (**13**), with its destabilizing

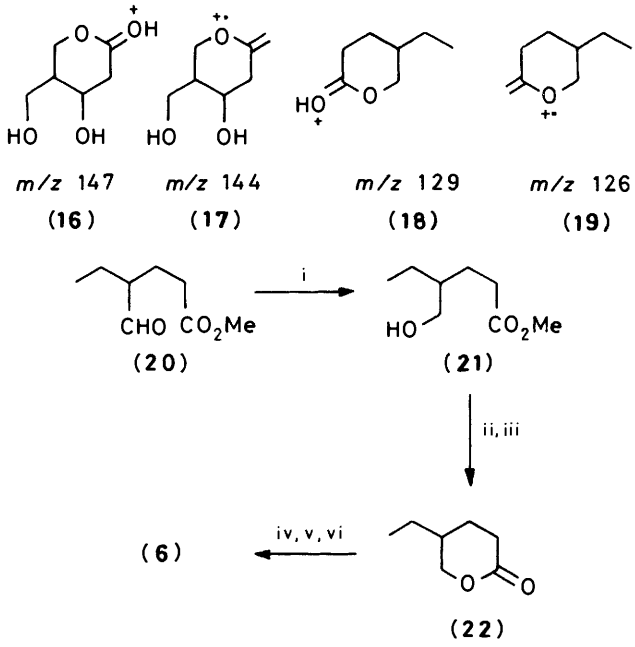


Scheme 3. *Reagents:* i, Bu^{t}Li–THF, 0 °C; ii, CuI–THF, −68 °C; iii, oxirane (**9**), 0—20 °C; iv, HCl–THF–water.

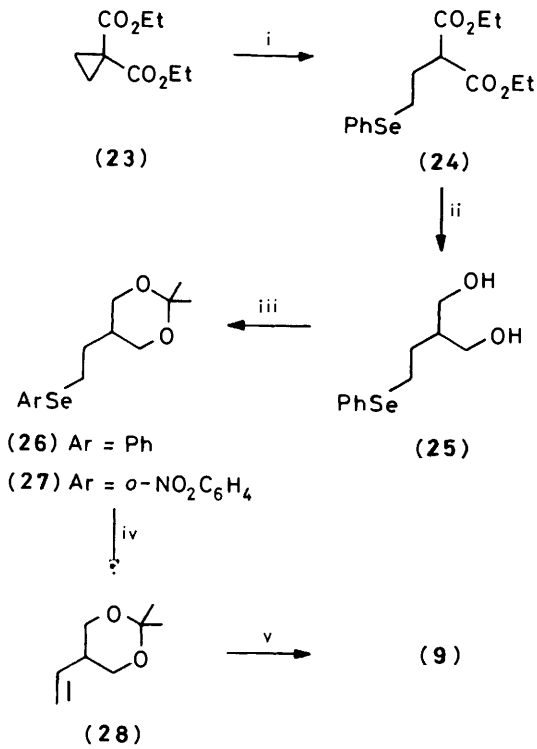
axial hydroxy function, decomposes slowly under the conditions used to hydrolyse (**10**). Nonetheless, pure crystalline talaromycin B can be prepared in gram quantities in modest overall yield from cheap, readily available starting materials. Attempts are now under way to extend the dihydropyran route to more complex spiroacetals.

Experimental

Column chromatography was carried out on Kieselgel 60 (230—400 mesh). All reactions requiring anhydrous conditions were conducted in flame-dried apparatus under a static atmosphere of dry nitrogen. Organic extracts were dried over $MgSO_4$ and evaporated at aspirator pressure using a Büchi rotary evaporator. Cuprous iodide was extracted with tetrahydrofuran in a Soxhlet apparatus and then dried at 0.5 mmHg. Commercial *m*-chloroperbenzoic acid containing 15—20% *m*-chlorobenzoic acid was used without further purification. Dry solvents were distilled from the appropriate dehydrating



Scheme 4. *Reagents:* i, PtO_2, $SnCl_2$–H_2–60% aq. EtOH; ii, NaOH, 20 °C; iii, conc. HCl; iv, Bu$^t_2$AlH–toluene, −78 °C; v, $MeSO_2Cl$–pyridine; vi, 100–110 °C, pyridine.



Scheme 5. *Reagents:* i, $PhSeBH_3Na$–EtOH; ii, $LiAlH_4$–Et_2O; iii, 2-methoxypropene, H^+; iv, H_2O_2–CH_2Cl_2–pyridine; v, *m*-$ClC_6H_4CO_3H$–CH_2Cl_2.

agents; THF (Na wire), EtOH [$Mg(OEt)_2$], CH_2Cl_2(P_2O_5), pyridine (CaH_2).

Chemical shifts are reported as δ values relative to tetramethylsilane as an internal standard. ^1H n.m.r. spectra were recorded at 90 MHz in $CDCl_3$ and i.r. spectra were obtained on thin films unless otherwise indicated. Peak

Table 1. 400 MHz ^{1}H n.m.r. data for talaromycin B (**12**), 4-*epi*-talaromycin B (**13**), and desethyltalaromycin B (**15**)[a]

	(12)	(13)	(15)
2-H_a	3.315 (dd, *J* 11, 11)	3.94 (dd, *J* 11.5, 11.5)	3.34 (dd, *J* 11.5, 11)
2-H_e	3.59 (dd, *J* 11, 5)	3.82 (dd, *J* 11.5, 4)	3.61 (dd, *J* 11.5, 5)
3-H_a	1.835 (tdt, *J* 11, 4.6, 6)	1.81 (m)	1.75—1.90 (m)
3-H_e	—	—	—
4-H_a	4.05 (ddd, *J* 11.5, 10.5, 5)	—	4.06 (ddd, *J* 11, 10.5)
4-H_e	—	4.16 (m)	—
5-H_a	1.44 (dd, *J* 12, 11)	1.68 (dd, *J* 14, 3.5)	1.41 (dd, *J* 12.5, 11)
5-H_e	1.99 (dd, *J* 12, 5)	1.92 (dd, *J* 14, 3.0)	2.02 (dd, *J* 12.5, 5)
8-H_a	3.195 (dd, *J* 11, 11)	3.34 (dd, *J* 11.5, 11.5)	3.52—3.63 unres.
8-H_e	3.51 (ddd, *J* 11, 4.5, 2)	3.72 (dd, *J* 11.5, 5)	3.52—3.63 unres.
9-H_a	1.43 (m)	1.4—1.7 unres.	1.48—1.57 unres.
9-H_e	—	—	1.75—1.90 (m)
10-H_a	1.38 (dq, *J* 13, 3.6)	1.4—1.7 unres.	1.48—2.57 unres.
10-H_e	1.60 (m)	1.4—1.7 unres.	1.59 (dm)
11-H_a	1.535 (ddd, *J* 13, 13, 4)	1.4—1.7 unres.	1.48—1.57 unres.
11-H_e	1.71 (ddd, *J* 13, 3.6, 2.5)	1.4—1.7 unres.	1.66 (dm)
12-H	*ca.* 3.68 (distorted d, *J ca.* 6)[b]	*ca.* 3.63 (m)	3.70—3.73 (m)
12-H′	*ca.* 3.68 (distorted d, *J ca.* 6)[b]	*ca.* 3.63 (m)	3.52—3.63 unres.
13-H_2	*ca.* 1.16 (m)	1.09—1.26 (m)	—
14-H_3	0.88 (t, *J* 7.5)	0.89 (t, *J* 7.5)	—

[a] Spectra were recorded in $CDCl_3$ solution; chemical shifts are given in p.p.m. relative to internal tetramethylsilane; coupling constants are given in Hz. [b] Reported as a doublet[9] in the 360 MHz spectrum. At 400 MHz these C-12 protons have a slightly different chemical shift giving rise to an ABX pattern. Abbreviations: q = quartet, t = triplet, d = doublet, m = multiplet, unres = unresolved, a = axial, e = equatorial.

Table 2. 22.5 MHz ^{13}C n.m.r. data for talaromycin B (**12**), 4-*epi*-talaromycin B (**13**), and desethyltalaromycin B (**15**)

	(12)	(13)	(15)
C-2	61.43	62.28	59.56 or 58.74
C-3	45.86	41.11	44.55
C-4	65.94	67.05	62.86
C-5	44.14	40.66	43.03
C-6	96.78	96.93	95.15
C-8	64.80	65.53	59.56 or 58.74
C-9	36.57	36.50	23.26
C-10	25.06 or 24.73	25.13 or 24.41	16.70
C-11	35.14	35.04	33.39
C-12	60.85	57.50	58.04
C-13	25.06 or 24.73	25.13 or 24.41	—
C-14	11.10	11.08	—

[a] Spectra were recorded in $CDCl_3$ solution; chemical shifts are given in p.p.m. relative to internal tetramethylsilane.

intensities are denoted by m (medium) and w (weak); otherwise, the signals are of strong intensity.

5-Ethyl-δ-valerolactone(*5-Ethyltetrahydro-2-pyrone*) (**22**).—A solution of the aldehyde (**20**)[15] (50 g, 0.316 mol) in 60% aqueous EtOH containing $SnCl_2$ (0.45 g, 2 mmol) was hydrogenated over $PtO_2 \cdot H_2O$ (0.5 g) at 1 atm. The mixture was periodically shaken in air for 5 min (*ca.* every 45 min) in order to increase the rate of reduction. After 3 h, the mixture was filtered through Celite and the EtOH removed under reduced pressure. The residue was diluted to 400 cm^3 with MeOH and 10M NaOH (40 cm^3) added dropwise. After 1 h the mixture was concentrated and the residue extracted with Et_2O (100 cm^3) which was discarded. The aqueous layer was acidified with concentrated HCl (32 cm^3) to pH 2—3 and stirred for 18 h. After saturation with salt, the mixture was extracted with CH_2Cl_2 (3 × 200 cm^3) and the combined extracts washed with saturated $NaHCO_3$, dried, and evaporated. Distillation of the residue gave (**22**) (25.4 g, 60%) as a colourless oil, b.p. 80—83 °C/0.7 mmHg; $\nu_{max.}$ 2 970, 1 740, 1 460, 1 405, 1 350, 1 340, 1 295, 1 240, 1 200, 1 185, 1 100, and 1 060 cm^{-1}; $\delta_H(CCl_4)$ 4.25 (1 H, m), 3.85 (1 H, dd, *J* 11, *J′* 9 Hz), 2.3—2.6 (2 H, m), 1.2—2.2 (5 H, m), and 0.95 (3 H, t, *J* 7 Hz).

3-Ethyl-3,4-dihydro-2H-pyran (**6**).—To a solution of the lactone (**22**) (25.7 g, 0.2 mol) in toluene (200 cm^3) cooled to −70 °C was added dropwise over 3 h, a solution of di-isobutylaluminium hydride (25% w/w; 225 cm^3, *ca.* 0.3 mol) in toluene. The mixture was stirred at −70 °C for a further 2 h and then poured into a mixture of glacial acetic acid (150 cm^3) and ice (300 g). After the mixture had been stirred for 15 min, the toluene layer was separated and the residue extracted with benzene (2 × 250 cm^3). The combined extracts were washed with saturated aqueous NaCl and $NaHCO_3$, dried, and evaporated to give 22 g (84%) of the lactol after distillation (b.p. 68—70 °C/1 mmHg.

To a solution of the lactol (17.8 g, 0.137 mol) in dry pyridine (200 cm^3) cooled to 0 °C under N_2 was added dropwise over 1 h, methanesulphonyl chloride (16 cm^3, 0.205 mol). The mixture was stirred at 0 °C for 1.5 h and then heated at 100—110 °C for a further 1.5 h. After cooling to room temperature the mixture was poured into water (500 cm^3) and extracted with light petroleum (b.p. 30—40 °C) (2 × 200 cm^3). The combined extracts were washed with water (4 × 500 cm^3), dried, and evaporated. Spinning band distillation of the residue gave (**6**) (9.02 g, 59%), b.p. 140—141 °C/759 mmHg; $\nu_{max.}$ 3 070m, 1 650, and 1 078 cm^{-1}; δ_H 6.3 (1 H, m), 4.65 (1 H, m), 4.0 (1 H, dd with further fine splitting, *J* 10, *J′* 2 Hz), 3.5 (1 H, dd with further fine splitting, *J* 10, *J′* 8 Hz), 1.15—2.2 (5 H, m), and 0.95 (3 H, distorted t, *J* 7 Hz) (Found: M^+, 112.0888. $C_7H_{12}O$ requires *M*, 112.088 81).

Diethyl 2-Phenylselenoethylmalonate (**24**).—To a solution of diphenyl diselenide (17.2 g, 55 mmol) in dry EtOH (200 cm^3) was added in portions at 0 °C, $NaBH_4$ (4.2 g, 111 mmol). To the cold, colourless solution was added dropwise over 30 min a solution of diethyl cyclopropane-1,1-dicarboxylate (18.6 g, 100 mmol) in EtOH (106 cm^3), and the mixture was stirred under N_2 for 18 h, acidified with 1M HCl (120 cm^3), diluted with water (300 cm^3), and the ethanol evaporated under reduced pressure.

The residue was extracted with benzene (2 × 300 cm^3) and dried. Chromatography on silica gel G (350 g) eluting with 0—15% EtOAc in light petroleum gave the selenide (**24**) as a yellow oil (32.9 g, 95%), $\nu_{max.}$ 2 990, 1 730, 1 575, 1 475, 1 435, 1 025, 860, 740, and 690 cm^{-1}; δ_H 7.0—7.6 (5 H, m), 4.1 (4 H, q, *J* 7 Hz), 3.53 (1 H, t, *J* 7 Hz), 2.90 (2 H, t, *J* 7 Hz), 2.25 (2 H, q, *J* 7 Hz), and 1.2 (6 H, t, *J* 7 Hz) (Found: M^+, 344.053 08. $C_{15}H_{20}O_4{}^{80}Se$ requires *M*, 344.052 620).

2-*Hydroxymethyl*-4-*phenylselenobutan*-1-*ol* (**25**).—Reduction of the ester (**24**) (32.9 g, 45 mmol) with $LiAlH_4$ in Et_2O in the usual way gave the diol (**25**) (27.4 g) which was used in the next step without further purification. A small sample was crystallized from Et_2O–hexane to give m.p. 48—49.5 °C, δ_H 7.1—7.6 (5 H, m), 2.96 (2 H, t, *J* 8 Hz), 2.7 (2 H, br, D_2O exchange), and 1.5—2.1 (3 H, m) (Found: C, 50.90; H, 6.3. $C_{11}H_{16}O_2Se$ requires C, 50.92; H, 6.22%).

2,2-*Dimethyl*-5-(2-*phenylselenoethyl*)-1,3-*dioxane* (**26**).—To a stirred solution of the crude diol (**25**) (27.4 g, 100 mmol) and toluene-*p*-sulphonic acid (20 mg) in CH_2Cl_2 (200 cm^3) was added dropwise at 0 °C 2-methoxypropene (11 cm^3, 110 mmol). The reaction was stirred at room temperature for 1.5 h, before anhydrous K_2CO_3 (2 g) was added and the mixture stirred for a further 30 min. Saturated brine (200 cm^3) was added and the organic layer separated. The aqueous layer was extracted with Et_2O (2 × 100 cm^3) and the combined organic extracts dried and evaporated to give (**26**) as a pale yellow oil (29.8 g, *ca.* 100%) which was used in the next step without further purification. A small sample purified by column chromatography on silica gel eluting with 10% Et_2O in light petroleum gave: $\nu_{max.}$ 1 580m, 1 480m, 1 200, 1 072, 830m, 738m, and 692m cm^{-1}; δ_H 7.25—7.5 (2 H, m), 7.05—7.25 (3 H, m), 3.8 (2 H, dd, *J* 4, *J'* 11 Hz), 3.42 (2 H, dd, *J* 7, *J'* 11 Hz), 2.84 (2 H, t, *J* 7 Hz), 1.4—2.0 (3 H, m), and 1.3 (6 H, s); *m/z* 300 (M^+, 20%), 285 (24), 184 (11), 171 (15), 158 (16), 157 (22), 143 (84), and 43 (100) (Found: M^+, 300.063 46. $C_{14}H_{20}O_2{}^{80}Se$ requires *M*, 300.062 791).

2,2-*Dimethyl*-5-*vinyl*-1,3-*dioxane* (**28**).—To a stirred solution of the crude selenide (**26**) (27.8 g, 93 mmol) in CH_2Cl_2 (300 cm^3) and pyridine (16 cm^3) was added dropwise at 0 °C over 30 min, 30% H_2O_2 (45 cm^3, 470 mmol). The mixture was allowed to warm to room temperature with occasional cooling to maintain the temperature at 15—20 °C. The mixture was stirred for a further 30 min and then added in one portion to refluxing CCl_4 (250 cm^3) containing pyridine (15 cm^3). After 15 min at reflux, the mixture was cooled, washed with saturated aqueous $NaHCO_3$ and the organic layer dried. The bulk of the solvent was removed at 160 mmHg (bath temperature 20 °C) and the residue was taken up in light petroleum (b.p. 30—40 °C, 100 cm^3), washed with water (3 × 100 cm^3), dried, and concentrated at 160 mmHg (bath temperature 20 °C). The residue was distilled to give the alkene (**28**) (4.3 g, 32%) as a colourless oil, b.p. 120—125 °C (bath)/140 mmHg; $\nu_{max.}$ 1 640w, 1 370, 1 245, 1 195, 1 150, 1 130, 1 065, 920, and 830 cm^{-1}; δ_H 5.4—5.8 (1 H, m), 5.05 (2 H, m), 3.78 (2 H, dd, *J* 11, *J'* 14 Hz), 3.68 (2 H, dd, *J* 11, *J'* 16 Hz), 2.3—2.8 (1 H, m), 1.42 (3 H, s), and 1.38 (3 H, s) (Found: M^+, 142.099 08; $C_8H_{14}O_2$ requires *M*, 142.099 373).

2,2-*Dimethyl*-5-*oxiranyl*-1,3-*dioxane* (**9**).—A mixture of *m*-chloroperbenzoic acid (7.5 g, 34 mmol), anhydrous $NaHCO_3$ (12 g), and olefin (**28**) (4.0 g, 28 mmol) in CH_2Cl_2 (50 cm^3) was stirred for 24 h. Saturated aqueous $NaHCO_3$ (50 cm^3) and $NaHSO_3$ (50 cm^3) were added and the mixture stirred for 30 min. The organic layer was separated and the aqueous layer extracted with CH_2Cl_2 (100 cm^3). The combined extracts were washed with $NaHCO_3$, dried, and evaporated. The residue was distilled to give the oxirane (**9**) (3.72 g, 85%) as a colourless oil, b.p. 110—115 °C (bath)/18 mmHg; $\nu_{max.}$ 1 268, 1 250, 1 200, and 830 cm^{-1}; δ_H 3.7—4.2 (4 H, m), 3.03 (1 H, ddd, *J* 7, *J'* 4.5, *J''* 4 Hz), 2.72 (1 H, dd, *J* 4.5, *J'* 4 Hz), 2.54 (1 H, dd, *J* 4.5, *J'* 3.0 Hz), 1.4 (6 H, s), and 1.4—1.7 (1 H, m) (Found: M^+, 158.0941. $C_8H_{14}O_3$ requires *M*, 158.094 288).

Talaromycin B (**12**) *and* 4-epi-*Talaromycin B* (**13**).—Bu^{t}Li (2.2M in pentane, 29 cm^3, 63.8 mmol) was added dropwise to a stirred solution of the dihydropyran (**6**) (5.3 g, 47.5 mmol) in dry THF (19 cm^3) at −68 °C. The mixture was then stirred at 0 °C for 1 h, cooled to −68 °C, and added rapidly *via* a cannula to a stirred suspension of CuI (5.26 g, 28 mmol) in THF (50 cm^3) at 68 °C. The black heterogeneous mixture was allowed to warm to −30 °C over 1 h and kept at −30 °C for 30 min. A solution of the oxirane (**9**) (2.5 g, 15.8 mmol) in THF (10 cm^3) was then added dropwise over 10 min. The mixture was allowed to warm slowly to room temperature and after 3 h was poured into saturated aqueous NH_4Cl containing 10% ammonia (150 cm^3). The mixture was extracted with Et_2O (3 × 75 cm^3) and the combined extracts washed with saturated NH_4Cl–ammonia, dried, and evaporated. The residue was allowed to stand at room temperature for 12 h in concentrated HCl–H_2O–THF (1:5:20) (80 cm^3), and was then neutralized with saturated aqueous $NaHCO_3$ and the bulk of the THF evaporated. The residue was extracted with CH_2Cl_2 (3 × 25 cm^3) and the combined extracts dried and evaporated. Thin layer chromatography [silica gel, triple elution with benzene–dioxane (3:1)] showed three major polar components having R_F 0.6, 0.43, and 0.37, which were separated by column chromatography on silica gel eluting with benzene–dioxane (5:2). The first component to elute was 4-*epi*-talaromycin B (**13**) (0.512 g, 14%), a colourless oil, $\nu_{max.}$ 3 450, 1 465, 1 432, 1 375, 1 180, 1 148, 1 090, 1 025, 1 015, and 900 cm^{-1}; *m/z* 230 (M^+, 6%), 147 (92), 144 (12), 129 (100), and 126 (72) (Found: M^+, 230.152 04. $C_{12}H_{22}O_4$ requires *M*, 230.151 180).

The second component to elute was talaromycin B (**12**) (0.85 g, 23%); m.p. (sealed tube) 135—136.5 °C (EtOAc–hexane); $\nu_{max.}$(KBr) 3 350, 1 380, 1 187, 1 085, 1 075, 1 060, 1 040, 1 035, 895, and 870 cm^{-1}; *m/z* 230 (M^+, 5%), 147 (100), 144 (99), 129 (80), and 126 (69) (Found: M^+, 230.151 36. $C_{12}H_{22}O_4$ requires *M*, 230.151 80) (Found: C, 62.45; H, 9.75. $C_{12}H_{22}O_4$ requires C, 62.58; H, 9.63%).

The third component to elute was obtained in *ca.* 5% yield and was identified as 3-hydroxy-2-hydroxymethyl-7,7-dimethyl-octan-1-ol, m.p. (sealed tube) 80—81 °C (EtOAc–hexane); $\nu_{max.}$($CHCl_3$) 3 620, 3 500, 1 470, 1 368, 1 072, and 950 cm^{-1}; δ_C 72.13, 62.41, 60.82, 46.68, 44.21, 35.92, 30.13, 29.42, and 21.06 (Found: C, 64.4; H, 11.7. $C_{11}H_{24}O_3$ requires C, 64.7; H, 11.8%). This product probably arose from the reaction of the oxirane (**9**) with 3,3-dimethylbutyl-lithium *via* the organocuprate. 3,3-Dimethylbutyl-lithium can be generated from the known[19] rapid addition of Bu^{t}Li with the ethylene which is a by-product of the decomposition of THF induced by Bu^{t}Li.[20]

Desethyltalaromycin B (**15**).—From 1.6 g (19 mmol) of 3,4-dihydro-2*H*-pyran (**1**) and 1.0 g (6.3 mmol) of the oxirane (**9**), desethyltalaromycin B (**15**) (0.633 g, 49%) was obtained as described above, m.p. (sealed tube) 127—129 °C; $\nu_{max.}$($CHCl_3$) 3 605m, 3 480br, 1 490, 1 385, 1 088, 900m, and 870 cm^{-1}; *m/z* 202 (M^+, 6%), 185 (16), 147 (35), 144 (19), 129 (24), 127 (19), 126 (24), 101 (100), and 98 (87) (Found: M^+, 202.120 82. $C_{10}H_{18}O_4$ requires *M*, 202.120 50) (Found: C, 59.65; H, 9.0. $C_{10}H_{18}O_9$ requires C, 59.4; H, 9.0%).

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