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An enantiospecific synthesis of (−)-talaromycins A and B from D-fructose*†

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ABSTRACT

(3*R*,4*R*,5*S*,6*R*,9*RS*)-9-Ethyl-3,4,5-trihydroxy-1,7-dioxaspiro[5.5]undecane (**9**) has been synthesised from 2,3:4,5-di-*O*-isopropylidene-β-D-fructopyranose (**3**) and transformed into (−)-talaromycin A (**1**). (−)-Talaromycin B (**2**) was obtained by isomerisation of **1** in acid medium.

INTRODUCTION

Since Lynn *et al.*[1] identified the (−)-talaromycins A (**1**) and B (**2**), isolated from the fungus *Talaromyces stipitatus*, several reports of enantioselective syntheses of such compounds have appeared[2–6].

Recently, Hough *et al.*[7] described the use of D-fructose derivatives as chiral precursors of simple spiroacetals. We now describe the synthesis of (−)-talaromycins A and B from 2,3:4,5-di-*O*-isopropylidene-β-D-fructopyranose[8] (**3**).

RESULTS AND DISCUSSION

Oxidation of **3** with pyridinium chlorochromate yielded 2,3:4,5-di-*O*-isopropylidene-β-D-*arabino*-hexos-2-ulo-2,6-pyranose (**4**), which was reacted with triphenyl(propionylmethylene)phosphorane[9] to afford (*E*)-1,2,4,5-tetradeoxy-6,7:8,9-di-*O*-isopropylidene-β-D-*arabino*-dec-4-eno-3,6-diulo-6,10-pyranose (**5**). The configuration at C-4,5 was shown to be *E* from the $J_{4,5}$ value (15.8 Hz). Partial hydrogenation (10% Pd–C) of **5** gave the ketone **6**, Wittig reaction of which with methylenetriphenylphosphorane produced 1,2,3,4,5-pentadeoxy-6,7:8,9-di-*O*-isopropylidene-3-*C*-methylene-β-D-*arabino*-dec-6-ulo-6,10-pyranose** (**7**). Hydroboration–oxidation of **7** produced an unresolvable mixture of C-3 epimers **8**. The ^{13}C-n.m.r. spectrum of **8** contained double signals for C-2,3′,4,5, which are close to the new chiral centre, but not for C-3.

* Dedicated to Professor Leslie Hough in the year of his 65th birthday.
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** In order to facilitate the numbering in n.m.r. spectra, these compounds are regarded as C-3 branched-chain sugar derivatives.

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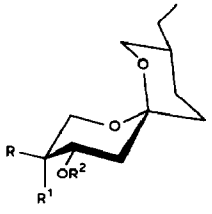
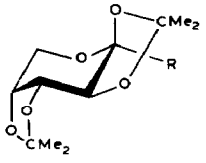
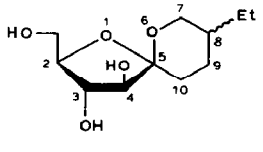
Spiroacetalation of **8** in an acid medium afforded a minor (**9a**) ($[\alpha]_D$ −28°) and a major spiroacetal (**9b**) ($[\alpha]_D$ −106°). The structure of the major component was assigned on the basis of its ^{13}C-n.m.r. data and on the studies of Deslongchamps *et al.*[10] on analogous compounds. The minor compound was (2*R*,3*R*,4*S*,5*R*,8*RS*)-8-ethyl-3,4-dihydroxy-2-hydroxymethyl-1,6-dioxaspiro[4.5]decane (**9a**), an isomer of **9b**, according to its ^{13}C-n.m.r. spectrum and the data in the literature[11]. Acetonation of each isomer led to a mixture of (3*R*,4*R*,5*S*,6*R*,9*S*)-9-ethyl-5-hydroxy-3,4-isopropylidenedioxy-1,7-dioxaspiro[5.5]undecane (**10**) and its 9*R* isomer (**11**), indicating that **9a** and **9b** were mixtures of epimers at the carbon atom bearing the ethyl group. The formation of **10** and **11** from **9a** could be explained by the fact that the geometrical disposition of the hydroxyl groups prevents their acetonation and, in the acid medium of the reaction, isomerisation to the more stable **9b** and subsequent acetonation could take place. ^{1}H-N.m.r. data of **10** and **11** established the configuration at C-9. Thus, for **11**, the resonance of H-8*a* was a triplet ($J_{8a,8e}$ = $J_{8a,9}$ = 10.8 Hz), indicating H-8*a*,9 to be *trans*-diaxial in accord with a 9*R* configuration, whereas, for **10**, it was a double doublet ($J_{8a,8e}$ 11, $J_{8a,9}$ 2.8 Hz), indicating H-8*a*,9 to be *cis* and the 9*S* configuration.



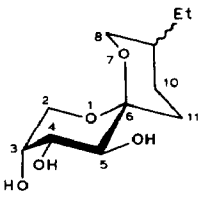
1 R = R^2 = H, R^1 = CH_2OH
2 R = CH_2OH, R^1 = R^2 = H
17 R, R^1 = =O, R^2 = Bn
18 R, R^1 = $=CH_2$, R^2 = Bn
19 R = OH, R^1 = Me, R^2 = Bn
20 R = H, R^1 = CH_2OH, R^2 = Bn



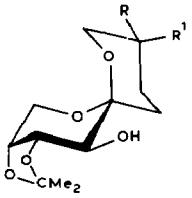
3 R = CH_2OH
4 R = CHO
5 R = *(E)*-CH=CHCOEt
6 R = $-CH_2-CH_2-COEt$
7 R = $-CH_2-CH_2-C(Et)=CH_2$
8 R = $-CH_2-CH_2-CH(Et)-CH_2OH$



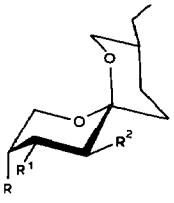
9a



9b



10 R = H, R^1 = Et
11 R = Et, R^1 = H



12 R = R^1 = O,O-CMe_2, R^2 = OCSSMe
13 R = R^1 = O,O-CMe_2, R^2 = H
14 R = R^1 = OH, R^2 = H
15 R = R^1 = O,O-$SnBu_2$, R^2 = H
16 R = OH, R^1 = OBn, R^2 = H

TABLE I

^{13}C-N.m.r. data for **5–8**

Compound	*C-1*	*C-2*	*C-3*	*C-4*	*C-5*	*C-6*	*C-7*	*C-8*	*C-9*	*C-10*	*CMe_2*	CMe_2	*C-3'*
5	7.85	34.16	200.81	129.50	142.81	101.45	73.49	70.43[a]	70.09[a]	61.33	108.92	24.17	
											109.24	24.86	
												25.91	
												26.18	
6	7.87	36.28[b]	211.17	35.96[b]	34.73	103.64	73.93	70.70[c]	70.56[c]	60.93	108.86	24.00	
											107.50	24.92	
												25.85	
												26.31	
7	12.42	29.39[d]	151.48	29.31[d]	39.37	104.10	73.88	70.89[e]	70.69[e]	60.96	108.92	24.13	107.03
											107.43	25.17	
												25.85	
												26.46	
8	10.98	23.35[f]	41.83	23.26[f]	37.76	104.28	73.78	70.82[g]	70.58[g]	60.91	108.89	24.06	64.89
		23.31[f]		23.18[f]	37.73						107.43	25.12	64.84
												25.78	
												26.42	

[a–g] Assignments may be interchanged.

TABLE II

^{13}C-N.m.r. data for **1**, **2**, **10–13**, **16**, and **18–20**

Compound	*C-2*	*C-3*	*C-4*	*C-5*	*C-6*	*C-8*	*C-9*	*C-10*	*C-11*	*C-12*	CH_2CH_3	CH_2CH_3	CMe_2	CMe_2	*C=S*	*SMe*	CH_2Ph	*Ph*
1	60.83	41.26	64.97	40.28	97.23	65.43	36.70	24.90	35.33	61.53	25.24	11.19						
2	60.46	45.43	67.83	44.07	97.23	65.30	36.72	24.79	35.21	62.81	25.21	11.17						
10	59.03	74.69[a]	73.82[a]	77.37	97.78	63.87	33.97	21.52	24.83		22.20	12.19	109.05	28.19 26.22				
11	58.98	74.29[b]	73.86[b]	77.41	97.54	66.32	36.30	29.91	24.44		25.17	11.12	109.06	28.23 26.25				
12	59.07	74.36[c]	74.32[c]	82.61	97.60	66.48	36.16	24.25	30.28		25.12	11.11	109.54	27.78 26.50	217.35	19.42		
13	59.97	71.77[d]	70.08[d]	34.44	96.36	65.95	36.70	24.84	35.66		25.28	11.20	108.45	28.05 27.91				
16	62.55	65.43	72.81	35.61[e]	97.08	65.65	36.77	24.76	35.13[e]		25.21	11.19					70.11	138.10 i- 128.53 m- 127.83 p- 127.66 o-
18	64.73	144.60	73.74	44.23	97.78	65.66	36.90	25.01	35.19	107.50	25.32	11.24					71.27	138.82 i- 128.46 m- 127.56 p- 127.39 o-
19	65.37	71.39	79.25	39.25	97.43	67.45	36.74	25.07	34.97	19.07	25.27	11.22					71.59	138.95 i- 128.48 m- 127.62 p- 127.48 o-
20	60.68	39.79	74.34	37.46	97.16	65.37	36.74	24.91	35.39	61.00	25.24	11.19					70.52	138.18 i- 128.51 m- 127.74 p- 127.54 o-

[a–e] Assignments may be interchanged.

Deoxygenation of **11** at C-5 was effected by Barton reduction[12] of the 5-xanthate **12**, to yield **13**. Hydrolysis of the 3,4-*O*-isopropylidene group in **13** gave the diol **14**. The 3,4-dibutylstannylenedioxy derivative (**15**) of **14** reacted regioselectively with benzyl bromide, and ring opening caused by equatorial attack[13] yielded **16**. Oxidation[14] at position 3 of **16** with pyridinium chlorochromate in the presence of molecular sieve 4 Å gave the ketone **17** (i.r. data), which reacted with methylenetriphenylphosphorane to afford (4*S*,6*R*,9*R*)-4-benzyloxy-9-ethyl-3-methylene-1,7-dioxaspiro[5.5]undecane (**18**).

Hydroboration–oxidation of **18** gave a mixture of (3*S*,4*S*,6*R*,9*R*)-4-benzyloxy-9-ethyl-3-hydroxy-3-methyl-1,7-dioxaspiro[5.5]undecane (**19**, 13.5%) and the 4-*O*-benzyl derivative (**20**, 58%) of (−)-talaromycin A (**1**). The structure and configuration of **20** was confirmed by hydrogenolysis which yielded **1** exclusively. These findings indicated that the hydroboration reaction proceeded by an equatorial attack. The n.m.r. data for **19** (see Experimental) confirmed the structure assigned. The assignment of configuration at C-3, based on the above-mentioned stereoselectivity, is tentative.

Acid-catalysed isomerisation of **1** with Amberlite IR-120 (H^+) resin in methanol gave (−)-talaromycin B (**2**, 92%).

EXPERIMENTAL

General methods. — Melting points were determined with an Electrothermal melting-point apparatus and are uncorrected. Solutions were dried over $MgSO_4$ before concentration under diminished pressure. The ^1H- and ^{13}C-n.m.r. spectra (300 MHz, internal Me_4Si) were recorded with a Bruker AM-300 spectrometer for solutions in $CDCl_3$. The assignment of resonances for **1**, **2** and **12** was assisted by ^{13}C–^1H COSY spectra. The ^{13}C-n.m.r. spectra were interpreted by using published[1] ^1H-n.m.r. data. I.r. spectra were recorded with a Perkin–Elmer 782 instrument and mass spectra with a Hewlett–Packard HP-5988-A spectrometer. Optical rotations were measured for solutions in chloroform (1-dm tube) with a Perkin–Elmer 141 polarimeter. G.l.c. was performed at 220° on a Perkin–Elmer 8410 gas chromatograph equipped with a flame-ionisation detector and a steel column (2 × 0.125 in. i.d.) packed with 5% of OV-17 on Chromosorb W (100–120 mesh). The N_2 flow rate was 30 mL/min, the injection port temperature was 250°, and the zone-detector temperature was 250°. T.l.c. was performed on Silica Gel G (Merck) with detection by charring with sulfuric acid. Column chromatography was performed on silica gel (Merck, 7734).

The non-crystalline compounds, for which elemental analyses were not obtained, were shown to be homogeneous by chromatography, and were characterised by n.m.r. and mass spectrometry.

*Oxidation of 2,3:4,5-di-*O*-isopropylidene-β-*D*-fructopyranose* (**3**). — To a stirred solution of **3** (ref. 8) (5.2 g, 20 mmol) in dry dichloromethane (100 mL) were added pyridinium chlorochromate (10 g, 44 mmol) and molecular sieve (4 Å, 10 g). Stirring was continued for 24 h at room temperature. G.l.c. (200°) then showed that **3** (*T* 4.83 min) had almost disappeared and that a new compound (*T* 3.08 min) was present. The mixture was diluted with ether (300 mL), filtered through silica gel G, and concentrated.

The residue was eluted from a short column of silica gel 60 with ether to give 2,3:4,5-di-*O*-isopropylidene-*β*-D-*arabino*-hexos-2-ulo-2,6-pyranose (**4**; 4 g, 77.5%) and its hydrated form (^{1}H-n.m.r. data).

Reaction of **4** *with triphenyl(propionylmethylene)phosphorane.* — To a solution of **4** (10 g, 38.7 mmol) in dry dichloromethane (30 mL) was added a solution of the ylid[9] (14 g, 42.2 mmol) in the same solvent (30 mL). T.l.c. (ether–hexane, 2:1) then revealed a new compound of higher mobility. The mixture was left for 24 h at room temperature, then concentrated, the residue was extracted with hexane (4 × 30 mL), and the combined extracts were concentrated. Column chromatography (ether–hexane, 1:3) of the residue gave (*E*)-1,2,4,5-tetradeoxy-6,7:8,9-di-*O*-isopropylidene-*β*-D-*arabino*-dec-4-eno-3,6-diulo-6,10-pyranose (**5**; 8.9 g, 74%), *T* 5.44 min, $[\alpha]_D$ −30° (*c* 1.16); ν_{max}^{film} 2991, 2942, and 2909 (C–H), 1706 and 1684 (C=O, conjugated ketone), 1647 (C=C, conjugated), 1383 and 1374 (CMe_2), 1253, 1213, 1176, 1114, 1072, 900, and 870 cm^{-1} (C–O–C and 1,3-dioxolane ring). ^{1}H-N.m.r. data: *δ* 6.67 and 6.11 (2 d, 2 H, $J_{4,5}$ 15.8 Hz, H-4,5), 4.58 (dd, 1 H, $J_{7,8}$ 2.6, $J_{8,9}$ 9 Hz, H-8), 4.21 (bdd, 1 H, H-9), 4.17 (d, 1 H, H-7), 3.88 (dd, 1 H, $J_{9,10a}$ 2, $J_{10a,10e}$ 13 Hz, H-10*a*), 3.76 (d, 1 H, H-10*e*), 2.56 (q, 2 H, $J_{1,2}$ 7.3 Hz, H-2,2), 1.53, 1.45, 1.34, and 1.31 (4 s, 12 H, 2 CMe_2), and 1.06 (t, 3 H, H-1,1,1). For the ^{13}C-n.m.r. data, see Table I. Mass spectrum: *m/z* 297 [52%, (M^+ − Me)], 2.54 [26, (M^+ − Me_2CO)], 239 [13, (M^+ − Me − Me_2CO)], 225 [7, (M^+ − Me_2CO − Et)], 197 [28, (M^+ − Me_2CO-COEt)], 179 [15, (M^+ − Me − Me_2CO − AcOH)], 167 (20), 151 (20), 111 (60), 85 (58, $C_4H_5O_2^+$), 83 (57), 67 (36), 59 (35, Me_2COH^+), 57 (55, $EtCO^+$), and 43 (100, Ac^+).

*1,2,4,5-Tetradeoxy-6,7:8,9-di-*O*-isopropylidene-β-*D-arabino-*deco-3,6-diulo-6,10-pyranose* (**6**). — A solution of **5** (8.8 g, 28.2 mmol) in methanol (50 mL) and triethylamine (0.3 mL) was hydrogenated at 1.5 atm. over 10% Pd–C (0.5 g). G.l.c. after 15 min revealed that **5** had disappeared and that a new compound (*T* 4.66 min) was present. The catalyst was collected and washed with methanol, and the combined filtrate and washings were concentrated. Chromatography (ether–hexane, 1:5) of the residue gave **6** (7.1 g, 80%), $[\alpha]_D$ −13° (*c* 1.35); ν_{max}^{film} 2989, 2942, and 2908 (C–H), 1718 (ketone, C=O), 1383 and 1375 (CMe_2), 1254, 1213, 1107, 1084, 1053, 900, and 871 cm^{-1} (C–O–C and 1,3-dioxolane ring). ^{1}H-N.m.r. data: *δ* 4.49 (dd, 1 H, $J_{7,8}$ 2.4, $J_{8,9}$ 8 Hz, H-8), 4.15 (dd, 1 H, $J_{9,10a}$ 1.2 Hz, H-9), 4.06 (d, 1 H, H-7), 3.77 (dd, 1 H, $J_{10a,10e}$ 13 Hz, H-10*a*), 3.64 (d, 1 H, H-10*e*), 2.75 (ddd, 1 H, $J_{4,5}$ 5.6, $J_{4,5'}$ 9.8, $J_{4,4'}$ 18 Hz, H-4), 2.64 (ddd, 1 H, $J_{4',5}$ 9.8, $J_{4',5'}$ 5.6 Hz, H-4′), 2.39 (q, 2 H, $J_{1,2}$ 7.3 Hz, H-2,2), 2.09 (ddd, 1 H, $J_{5,5'}$ 14 Hz, H-5), 1.94 (ddd, 1 H, H-5′), 1.44, 1.43, and 1.28 (3 s, 3, 3, and 6 H, 2 CMe_2), and 1.13 (t, 3 H, H-1,1,1). For the ^{13}C-n.m.r. data, see Table I. Mass spectrum: *m/z* 314 (9%, M^+), 299 [32, (M^+ − Me)], 256 [2, (M^+ − Me_2CO)], 241 [3, (M^+ − Me − Me_2CO)], 227 [7, (M^+ − Me_2CO − Et)], 199 [6, (M^+ − Me_2CO − COEt)], 181 [26, (M^+ − Me − Me_2CO − AcOH)], 169 (10), 143 (7), 125 (10), 113 (68), 85 (32, $C_4H_5O_2^+$), 59 (34, Me_2COH^+), 57 (98, $EtCO^+$), and 43 (100, Ac^+).

Reaction of **6** *with methylenetriphenylphosphorane.* — To a stirred solution of imidazole (150 mg) in dry methyl sulfoxide (45 mL) was added sodium hydride (1.5 g, 50 mmol, 80% dispersion in oil) under N_2. After 15 min, methyltriphenylphosphonium

bromide (26.7 g, 75 mmol) was added, the mixture was stirred for 30 min at room temperature, and a solution of **6** (9.2 g, 29.3 mmol) in anhydrous ether (40 mL) was added dropwise. T.l.c. (ether–hexane, 2:1) then revealed the presence of a new compound of higher mobility. The mixture was left for 5 h at room temperature, then poured into ice–water, and extracted with ether, and the extract was washed with brine and water, and concentrated. The residue was extracted with hexane (4 × 25 mL), the combined extracts were concentrated, and the residue was chromatographed (ether–hexane, 1:4) to yield 1,2,3,4,5-pentadeoxy-6,7:8,9-di-*O*-isopropylidene-3-*C*-methylene-*β*-D-*arabino*-deco-6-ulo-6,10-pyranose (**7**, 8.5 g, 93%) as a clear mobile oil, $[\alpha]_D$ −14° (*c* 1); ν_{max}^{film} 2990, 2939, and 2904 (C–H), 1648 (C=C), 1383 and 1373 (CMe_2), 1253, 1212, 1189, 1171, 1107, 1068, 980, 900, and 874 cm^{-1} (C–O–C and 1,3-dioxolane ring). ^{1}H-N.m.r. data: δ 4.68 (bs, 2 H, H-3′,3′), 4.59 (dd, 1 H, $J_{7,8}$ 2.4, $J_{8,9}$ 8.4 Hz, H-8), 4.19 (bdd, 1 H, H-9), 4.09 (d, 1 H, H-7), 3.83 (dd, 1 H, $J_{9,10a}$ 2, $J_{10a,10e}$ 13 Hz, H-10*a*), 3.70 (d, 1 H, H-10*e*), 2.34 and 2.21 (2 dt, 2 H, H-4,4′), 2.01 (bq, 2 H, $J_{1,2}$ 7.4 Hz, H-2,2), 1.97 (dt, 1 H, $J_{4,5}$ 4.7, $J_{4',5} = J_{5,5'} = 13$ Hz, H-5), 1.82 (dt, 1 H, $J_{4',5'}$ 4.7, $J_{4,5'}$ 13 Hz, H-5′), 1.49, 1.46, 1.33, and 1.32 (4 s, 12 H, 2 CMe_2), and 1.00 (t, 3 H, H-1,1,1). For the ^{13}C-n.m.r. data, see Table I. Mass spectrum: *m/z* 312 (2%, M^+), 297 [19, $(M^+ - Me)$], 254 [8, $(M^+ - Me_2CO)$], 239 [3, $(M^+ - Me - Me_2CO)$], 237 [7, $(M^+ - Me - AcOH)$], 229 [21, $(M^+ - C_6H_{11})$], 196 (9), 179 [14, $(M^+ - Me - Me_2CO - AcOH)$], 171 [17, $(M^+ - C_6H_{11} - Me_2CO)$], 161 (23), 143 (43), 123 (30), 113 (17, $C_6H_9O_2^+$), 111 (40), 85 (40, $C_4H_5O_2^+$), 59 (51, Me_2COH^+), and 43 (100, Ac^+).

Hydroboration–oxidation of **7**. — To an ice-cooled and stirred solution of **7** (9.81 g, 31.4 mmol) in anhydrous tetrahydrofuran (30 mL) was added, dropwise under N_2, M BH_3-tetrahydrofuran in the same solvent (12 mL). The mixture was left for 2 h at room temperature, then 3M NaOH (15 mL) and aqueous 30% H_2O_2 (15 mL) were added dropwise at 0–30° with stirring and ice-cooling. Stirring was continued for 1 h at room temperature and for 1 h at 35–40°. The mixture was saturated with K_2CO_3, the organic layer was separated, the aqueous layer was extracted with ether (3 × 20 mL), and the combined extracts were washed with brine and concentrated. Chromatography (ether–hexane, 2:3 → 2:1) of the residue gave a mixture (8.24 g, 86%) of 1,2,3,4,5-pentadeoxy-3-*C*-hydroxymethyl-6,7:8,9-di-*O*-isopropylidene-*β*-D-*gluco*- and -D-*manno*-deco-6-ulo-6,10-pyranose (**8**), $[\alpha]_D$ −12° (*c* 1); ν_{max}^{film} 3466 (OH), 2989, 2963, and 2939 (C–H), 1383 and 1373 (CMe_2), 1254, 1212, 1175, 1107, 1069, 988, and 899 cm^{-1} (C–O–C and 1,3-dioxolane ring). ^{1}H-N.m.r. data: δ 4.52 (dd, 1 H, $J_{7,8}$ 2.4, $J_{8,9}$ 8 Hz, H-8), 4.17 (bdd, 1 H, H-9), 4.06 (d, 1 H, H-7), 3.80 (dd, 1 H, $J_{9,10a}$ 2, $J_{10a,10e}$ 13 Hz, H-10*a*), 3.67 (d, 1 H, H-10*e*), 3.50 (bd, 2 H, CH_2OH), 1.91–1.25 (m, 8 H, H-2,2,3,4,4′,5,5′ and HO), 1.47, 1.44, 1.31, and 1.30 (4 s, 12 H, 2 CMe_2), and 0.85 (t, 3 H, $J_{1,2}$ 7.4 Hz, H-1,1,1). For the ^{13}C-n.m.r. data, see Table I. Mass spectrum: *m/z* 330 (0.4%, M^+), 315 [29.7, $(M^+ - Me)$], 300 [6.7, $(M^+ - H_2CO)$], 272 [1.3, $(M^+ - Me_2CO)$], 255 [12.8, $(M^+ - Me - AcOH)$], 229 [7.3, $(M^+ - C_6H_{13}O)$], 197 [14.6, $(M^+ - Me - AcOH - Me_2CO)$], 179 [19.0, $(M^+ - Me - AcOH - Me_2CO - H_2O)$], 171 [12.0, $(M^+ - C_6H_{13}O - Me_2CO)$], 143 (36.0), 129 (83.7), 111 (41.6), 85 (32.3, $C_{11}H_5O_2^+$), 59 (59.9, Me_2COH^+), and 43 (100, Ac^+).

(*3*R,*4*R,*5*S,*6*R,*9*S)-*9-Ethyl-5-hydroxy-3,4-isopropylidenedioxy-1,7-dioxaspiro-*

[5.5]undecane (**10**) *and its 9-epimer* (**11**). — A solution of **8** (8.24 g, 25 mmol) in aqueous 70% trifluoroacetic acid (50 mL) was kept at room temperature overnight. T.l.c. (chloroform–methanol, 5:1) then revealed the absence of **8** and the presence of two new compounds of lower mobility. The mixture was concentrated, and water and then dichloromethane were distilled repeatedly from the residue. Column chromatography (chloroform → chloroform–methanol, 10:1) then gave a minor fraction identified as (2*R*,3*R*,4*S*,5*R*,8*RS*)-8-ethyl-3,4-dihydroxy-2-hydroxymethyl-1,6-dioxaspiro[4.5]decane (**9a**, 400 mg), $[\alpha]_D$ −28° (*c* 1). ^{13}C-N.m.r. data [$(CD_3)_2SO$]: δ 104.98 (C-5), 83.42 (C-2), 81.49 (C-4), 78.09 (C-3), 64.95 (C-7), 61.42 (CH_2OH), 36.53 (C-8), 29.31 (C-10), 24.94 and 24.76 (C-9 and CH_2CH_3), 10.98 (CH_2CH_3).

Eluted second was (3*R*,4*R*,5*S*,6*R*,9*RS*)-9-ethyl-3,4,5-trihydroxy-1,7-dioxaspiro[5.5]undecane (**9b**, 4.74 g), $[\alpha]_D$ −106° (*c* 1). ^{13}C-N.m.r. data [$(CD_3)_2SO$]: δ 98.09 (C-6), 71.73 (C-3), 69.27 and 69.07 (C-4,5), 64.69 (C-8), 62.75 (C-2), 36.05 (C-9), 29.82 (C-11), 24.80 and 24.45 (C-10 and CH_2CH_3), and 11.02 (CH_2CH_3).

To a stirred solution of **9b** (4.74 g) in dry acetone (60 mL) was added anhydrous copper sulfate (6 g) and *p*-toluenesulfonic acid (700 mg), and the mixture was kept at room temperature. After 4 days, t.l.c. (ether–hexane, 3:2) revealed traces of **9b** and two new compounds of higher mobility. The mixture was neutralised (K_2CO_3), filtered, and concentrated.

The minor fraction (**9a**, 400 mg) was treated with acetone (10 mL), anhydrous copper sulfate (1 g), and *p*-toluenesulfonic acid (100 mg) as described above. T.l.c. showed the same result, and the mixture was processed in a similar manner.

The combined residues (6.8 g), after repeated column chromatography (ether–hexane, 1:4 → 2:1) and recrystallisations (hexane), afforded **10** (1.6 g, 22.6%), m.p. 107–109° (from hexane), $[\alpha]_D$ −164° (*c* 1); ν_{max}^{KBr} 3461 (OH), 2964, 2938, and 2878 (C–H), 1385 and 1368 (CMe_2), 1251, 1228, 1220, 1107, 1069, 940, and 856 cm^{-1} (C–O–C and 1,3-dioxolane ring). ^{1}H-N.m.r. data: δ 4.15 (dd, 1 H, $J_{3,4}$ 5.7, $J_{2e,3}$ 2.6 Hz, H-3), 4.05 (dd, 1 H, H-4), 3.94 (d, 1 H, $J_{2a,2e}$ 13.3 Hz, H-2*a*), 3.79 (dd, 1 H, H-2*e*), 3.73 (dd, 1 H, $J_{8a,9}$ 2.8, $J_{8a,8e}$ 11 Hz, H-8*a*), 3.48 (bd, 1 H, H-8*e*), 3.29 (t, 1 H, $J_{4,5} = J_{5,OH}$ = 9 Hz, H-5), 2.20 (d, 1 H, HO-5), 2.12 (dt, 1 H, $J_{10e,11a}$ 4.7, $J_{10a,11a} = J_{11a,11e}$ = 13.7 Hz, H-11*a*), 1.94 (tt, 1 H, $J_{10a,10e}$ 13.7, $J_{9,10a} = J_{10a,11e}$ = 4.2 Hz, H-10*a*), 1.62–1.24 (m, 5 H, H-9,10*e*,11*e* and CH_2CH_3), 1.48 and 1.31 (2 s, 6 H, CMe_2), and 0.87 (t, 3 H, *J* 7.3 Hz, CH_2CH_3). For the ^{13}C-n.m.r. data, see Table II. Mass spectrum: *m/z* 272 (2.5%, M^+), 257 [9.7, $(M^+ - Me)$], 243 [4.5, $(M^+ - Et)$], 213 (1.9), 187 (4.3), 142 (9.4), 129 (100, $C_7H_{13}O_2^+$), 111 (45.8), 100 (50.9, $C_5H_8O_2^+$), 85 (74.8, $C_4H_5O_2^+$), and 69 (26.3).

Anal. Calc. for $C_{14}H_{24}O_5$: C, 61.74; H, 8.88. Found: C, 61.80; H, 8.90.

Eluted second was **11** (2.4 g, 40%), m.p. 77–79° (from hexane) $[\alpha]_D$ −147° (*c* 1); ν_{max}^{KBr} 3420 (OH), 2984, 2967, 2941, and 2874 (C–H), 1382 and 1372 (CMe_2), 1233, 1218, 1168, 1119, 1094, 1079, and 994 cm^{-1} (C–O–C and 1,3-dioxolane ring). ^{1}H-N.m.r. data: δ 4.17 (dd, 1 H, $J_{3,4}$ 5.7, $J_{2e,3}$ 2.7 Hz, H-3), 4.00 (dd, 1 H, H-4), 3.94 (d, 1 H, $J_{2a,2e}$ 13.4 Hz, H-2*a*), 3.79 (dd, 1 H, H-2*e*), 3.62 (ddd, 1 H, $J_{8e,9}$ 4, $J_{8e,10e}$ 2 Hz, H-8*e*), 3.37 (t, 1 H, $J_{4,5} = J_{5,OH}$ = 7.5 Hz, H-5), 3.19 (t, 1 H, $J_{8a,8e} = J_{8a,9}$ = 10.8 Hz, H-8*a*), 2.43 (d, 1 H, HO-5), 1.99

(dt, 1 H, $J_{10e,11a}$ 4.7, $J_{11a,11e} = J_{10a,11a}$ = 13.3 Hz, H-11*a*), 1.64 (dm, H-10*e*), 1.54 (dbt, 1 H, H-11*e*), 1.49 and 1.32 (2 s, 6 H, CMe_2), 1.50–1.34 (m, 2 H, H-9,10*a*), 1.11 (m, 2 H, CH_2CH_3), and 0.84 (t, 3 H, *J* 7.4 Hz, CH_2CH_3). For the ^{13}C-n.m.r. data, see Table II. Mass spectrum: *m/z* 272 (6.5%, M^+), 257 [9.4, ($M^+ - Me$)], 213 (2.1), 187 (3.9), 142 (8.4), 129 (100, $C_7H_{13}O_2^+$), 111 (35.2), 101 (23.7), 100 (44.5, $C_5H_8O_2^+$), 85 (66.4, $C_4H_5O_2^+$), and 69 (20.5).

Anal. Found: C, 61.53; H, 9.01.

(3R,4R,5S,6R,9R)-9-Ethyl-3,4-isopropylidenedioxy-5-[(methylthio)thiocarbonyloxy]-1,7-dioxaspiro[5.5]undecane (**12**). — A solution of **11** (2.4 g, 8.82 mmol) in anhydrous tetrahydrofuran (20 mL) was added to a stirred solution of $NaCH_2SOMe$ (from 530 mg of an 80% dispersion of sodium hydride in oil) and imidazole (50 mg) in anhydrous methyl sulfoxide (5 mL) under N_2 at room temperature. The mixture was heated for 15 min at 40–50° and then cooled, methyl iodide (1.8 mL, 37 mmol) was added slowly, and the mixture was heated for 30 min at 60°. T.l.c. (ether–hexane, 3:2) then revealed that **11** had disappeared to give a faster running product. The excess of the hydride was destroyed by the addition of ether saturated with water and then water. The organic phase was separated, the aqueous phase was extracted with ether, and the combined extracts were washed with brine and water, and concentrated. Chromatography (ether–hexane, 1:4) of the residue gave **12** (3.15 g, quantitative), m.p. 103–105° (from hexane), $[\alpha]_D$ −247° (*c* 1.1); ν_{max}^{KBr} 2980, 2963, 2933, and 2879 (C–H), 1383 and 1372 (CMe_2), 1274, 1245, 1221, 1204 (C=S), 1181, 1120, 1083, 1072, 1032, 992, and 850 cm^{-1} (C–O–C, C–S and 1,3-dioxolane ring). ^{1}H-N.m.r. data: δ 5.89 (d, 1 H, $J_{4,5}$ 8 Hz, H-5), 4.42 (dd, 1 H, $J_{3,4}$ 5.4 Hz, H-4), 4.28 (dd, 1 H, $J_{2e,3}$ 2.6 Hz, H-3), 4.03 (d, 1 H, $J_{2a,2e}$ 13.4 Hz, H-2*a*), 3.86 (dd, 1 H, H-2*e*), 3.67 (ddd, 1 H, $J_{8e,9}$ 4, $J_{8e,10e}$ 2 Hz, H-8*e*), 3.18 (t, 1 H, $J_{8a,8e} = J_{8a,9}$ = 10.7 Hz, H-8*a*), 2.57 (s, 3 H, SMe), 1.68–1.35 (m, 5 H, H-9,10*a*,10*e*,11*a*, 11*e*), 1.62 and 1.33 (2 s, 6 H, CMe_2), 1.13 (dquin, 2 H, CH_2CH_3), and 0.85 (t, 3 H, *J* 7.4 Hz, CH_2CH_3). For the ^{13}C-n.m.r. data, see Table II. Mass spectrum: *m/z* 347 [0.9%, ($M^+ - Me$)], 287 [2.6, ($M^+ - Me - AcOH$)], 255 [19.3, ($M^+ - OCSSMe$)], 254 [75.4, ($M^+ - OCS - MeSH$)], 224 (46.3), 196 [17.0, ($M^+ - OCS - MeSH - Me_2CO$)], 195 (24.3), 171 (52.7), 168 (100), 143 (29.5), 91 (49.3, $MeSCS^+$), 85 (27.4, $C_4H_5O_2^+$), and 69 (41.0).

Anal. Calc. for $C_{16}H_{26}O_5S_2$: C, 53.01; H, 7.23: Found: C, 53.20; H, 7.28.

(3R,4S,6R,9R)-9-Ethyl-3,4-isopropylidenedioxy-1,7-dioxaspiro[5.5]undecane (**13**). — A solution of **12** (3.9 g, 10.77 mmol) and azo-bis(isobutyronitrile) (50 mg) in dry toluene (25 mL) was added dropwise to a stirred boiling solution of tributyltin hydride (4.5 mL, 15.5 mmol) in the same solvent (25 mL) under N_2. Boiling under reflux was continued overnight. T.l.c. (ether–hexane, 3:2) then revealed no **12** but a new compound of lower mobility. The mixture was concentrated and the residue was chromatographed (ether–hexane, 1:4) to afford **13** (2.31 g, 84%) as a colourless syrup, $[\alpha]_D$ −101° (*c* 1); ν_{max}^{film} 2963, 2939, and 2876 (C–H), 1381 and 1371 (CMe_2), 1241, 1216, 1121, 1073, 995, and 874 cm^{-1} (C–O–C and 1,3-dioxolane ring). ^{1}H-N.m.r. data: δ 4.38 (dt, 1 H, $J_{3,4} = J_{4,5e}$ = 6, $J_{4,5a}$ 8.3 Hz, H-4), 4.05 (bdd, 1 H, H-3), 3.92 (bd, 1 H, $J_{2a,2e}$ 13.3 Hz, H-2*a*), 3.78 (dd, 1 H, $J_{2e,3}$ 2.6 Hz, H-2*e*), 3.51 (ddd, 1 H, $J_{8e,9}$ 3.8, $J_{8e,10e}$ 1.8 Hz, H-8*e*), 3.21 (t, 1 H, $J_{8a,8e} = J_{8a,9}$

= 11 Hz, H-8*a*), 1.85 (dd, 1 H, $J_{5a,5e}$ 13.7 Hz, H-5*e*), 1.66 (dd, 1 H, H-5*a*), 1.85–1.79, 1.64–1.53, and 1.45–1.37 (3 m, 4 H, H-9,10*e*,10*a*,11*e*), 1.48 and 1.31 (2 s, 6 H, CMe_2), 1.30 (dt, 1 H, $J_{11a,11e} = J_{10a,11a} = 16$, $J_{10e,11a}$ 7.7 Hz, H-11*a*), 1.12 (m, 2 H, CH_2CH_3), and 0.85 (t, 3 H, *J* 7.4 Hz, CH_2CH_3). For the ^{13}C-n.m.r. data, see Table II. Mass spectrum: *m/z* 241 [13%, $(M^+ - Me)$], 226 [4, $(M^+ - H_2CO)$], 181 [23, $(M^+ - Me - AcOH)$], 173 (45), 155 (27), 129 (15, $C_7H_{13}O_2^+$), 115 (27), 100 (100, $C_5H_8O_2^+$), 85 (55, $C_4H_5O_2^+$), 59 (15, Me_2COH^+), and 43 (19, Ac^+).

(3R,4S,6R,9R)-4-Benzyloxy-9-ethyl-3-hydroxy-1,7-dioxaspiro[5.5]undecane (**16**). — A solution of **13** (2.25 g, 8.8 mmol) in aqueous 60% acetic acid (13 mL) was heated for 1 h at 50°. T.l.c. (ethyl acetate) then revealed the presence of a new compound of lower mobility. The mixture was concentrated and toluene was evaporated repeatedly from the residue in order to remove acetic acid. Column chromatography (ethyl acetate) then afforded the diol **14** (1.62 g, 85.3%). To a solution of **14** (1.62 g, 7.5 mmol) in anhydrous methanol (20 mL) was added dibutyltin oxide (2 g, 8 mmol), and the suspension was heated for 2 h under reflux, then concentrated to afford the 3,4-dibutylstannylene derivative **15** as a syrup that was dried under vacuum over P_2O_5 overnight. A solution of **15** in dry *N,N*-dimethylformamide (25 mL) was treated with benzyl bromide (2.7 mL, 23 mmol) and heated at 110–120° for 2 h. T.l.c. (ether–hexane, 1:1) then revealed a main faster running product. Evaporation of the solvent gave a residue, a solution of which in dichloromethane (50 mL) was washed with brine and water, and concentrated. Column chromatography (ether–hexane, 1:3) of the residue afforded **16** (1.8 g, 78.6%), as a syrup, $[\alpha]_D$ −56° (*c* 1); ν_{max}^{film} 3441 (OH), 3067 and 3034 (C–H, aromatic), 2963, 2934, and 2875 (C–H), 1455 (benzyl), 1373, 1216, 1184, 1098, 1071, 992, and 886 (C–O–C), 737 and 698 cm^{-1} (aromatic). ^{1}H-N.m.r. data: δ 7.32 (s, 5 H, CH_2Ph), 4.56 (s, 2 H, CH_2Ph), 3.90 (bd, 1 H, H-3), 3.88 (dt, 1 H, $J_{3,4} = J_{4,5e} = 3.2$, $J_{4,5a}$ 9.2 Hz, H-4), 3.80 (dd, 1 H, $J_{2a,2e}$ 12.2, $J_{2a,3}$ 1.8 Hz, H-2*a*), 3.64 (bd, 1 H, H-2*e*), 3.51 (dm, 1 H, H-8*e*), 3.20 (t, 1 H, $J_{8a,8e} = J_{8a,9} = 11$ Hz, H-8*a*), 2.45 (bs, 1 H, HO-3), 1.90–1.35 (m, 7 H, H-5*a*,5*e*,9,10*a*,10*e*,11*a*,11*e*), 1.14 (dquin, 2 H, CH_2CH_3), and 0.86 (t, 3 H, *J* 7.4 Hz, CH_2CH_3). For the ^{13}C-n.m.r. data, see Table II. Mass spectrum: *m/z* 307 [0.5%, $(M^+ + 1)$], 306 (2.5, M^+), 291 [0.2, $(M^+ - Me)$], 288 [0.6, $(M^+ - H_2O)$], 277 [0.1, $(M^+ - Et)$], 245 (6.5), 223 (1.9), 185 (5.6), 155 (14.4), 129 (13.6, $C_7H_{13}O_2^+$), 127 (27.2), 91 (100, $C_7H_7^+$), and 57 (9.4).

(4S,6R,9R)-4-Benzyloxy-9-ethyl-3-methylene-1,7-dioxaspiro[5.5]undecane (**18**). — To a stirred and cooled (ice–water) solution of **16** (1.7 g, 5.5 mmol) in dry dichloromethane (25 mL) were added sodium acetate (180 mg, 219 mmol), molecular sieve (4 Å, powder, 2.5 g), and pyridinium chlorochromate (2.4 g, 11 mmol). Stirring was maintained at room temperature for 2.5 h. T.l.c. (ether–hexane, 2:1) then revealed a new compound of higher mobility. The mixture was diluted with ether (30 mL), filtered through silica gel G, and concentrated to give **17** (1.18 g); ν_{max}^{film} 3067 and 3036 (C–H, aromatic), 2964, 2936, and 2876 (C–H), 1737 (C=O, ketone), 1455 (benzyl), 1205, 1185, 1129, 1115, 1092, 1046, 992, and 870 (C–O–C), 745 and 698 cm^{-1} (aromatic).

To a stirred solution of $NaCH_2SOMe$ (from 300 mg of an 80% dispersion of sodium hydride in oil) and imidazole (50 mg) in anhydrous methyl sulfoxide (15 mL)

under N_2 was added methyltriphenylphosphonium bromide (3.5 g, 9.8 mmol). The mixture was stirred for 15 min and a solution of **17** (1.18 g) in dry ether (15 mL) was added dropwise. T.l.c. (ether–hexane, 2:1) then revealed a new compound of higher mobility. The mixture was left for 2 h at room temperature, and ether saturated with water was added. The organic phase was separated, the aqueous phase was extracted with ether, and the combined extracts were washed with brine and water, and concentrated. Chromatography (ether–hexane, 1:3) of the residue gave **18** (580 mg, 35% from **16**) as a colourless syrup, $[\alpha]_D$ −70° (*c* 1); ν_{max}^{film} 3067 and 3035 (C–H, aromatic), 2963, 2931, and 2861 (C–H), 1664 (C=C), 1455 (benzyl), 1181, 1127, 1088, 1041, 1034, and 909 (C–O–C), 734 and 696 cm^{-1} (aromatic). ^{1}H-N.m.r. data: δ 7.36 (s, 5 H, CH_2Ph), 5.23 (t, 1 H, $J_{12,12'} = J_{4,12}$ = 2 Hz, H-12), 5.00 (d, 1 H, H-12'), 4.66 and 4.60 (2 d, 2 H, *J* 12 Hz, CH_2Ph), 4.36 (m, 1 H, H-4), 4.15 (bd, 1 H, $J_{2a,2e}$ 12 Hz, H-2*a*), 3.97 (d, 1 H, H-2*e*), 3.57 (ddd, 1 H, $J_{8e,9}$ 4, $J_{8e,10e}$ 2 Hz, H-8*e*), 3.28 (t, 1 H, $J_{8a,8e} = J_{8a,9}$ = 10.8 Hz, H-8*a*), 2.23 (dd, 1 H, $J_{4,5e}$ 5.4, $J_{5a,5e}$ 12.3 Hz, H-5*e*), 1.80–1.10 (m, 8 H, H-5*a*,9,10*a*,10*e*,11*a*,11*e* and CH_2CH_3), and 0.90 (t, 3 H, *J* 7.4 Hz, CH_2CH_3). For the ^{13}C-n.m.r. data, see Table II. Mass spectrum: *m/z* 303 [0.3%, $(M^+ + 1)$], 302 (1.0, M^+), 287 [0.2, $(M^+ - Me)$], 284 (1.1), 219 (10.3), 211 (14.2), 159 (7.0), 129 (28.9, $C_7H_{13}O_2^+$), 111 (17.5), 91 (100, $C_7H_7^+$), and 65 (7.5).

Hydroboration–oxidation of **18**. — To an ice-cooled and stirred solution of **18** (530 mg, 1.74 mmol) in anhydrous tetrahydrofuran (10 mL) was added, dropwise under N_2, M BH_3-tetrahydrofuran in the same solvent (1 mL). The mixture was stirred for 30 min at −15°, then for 3 h at room temperature. 3M NaOH (1 mL) and aqueous 30% H_2O_2 (1 mL) were added dropwise to the stirred and ice-cooled mixture. Stirring was continued for 30 min at room temperature, ether (10 mL) was added, the organic phase was separated, and the aqueous phase was extracted with ether. The combined extracts were washed with brine and water, and concentrated. Chromatography (ether–hexane, 1:2) of the residue gave, first, (3*S*,4*S*,6*R*,9*R*)-4-benzyloxy-9-ethyl-3-hydroxy-3-methyl-1,7-dioxaspiro[5.5]undecane (**19**; 75 mg, 13.5%) as a colourless oil, $[\alpha]_D$ −63° (*c* 1); ν_{max}^{film} 3450 (OH), 3068 and 3034 (C–H, aromatic), 2964, 2938, and 2877 (C–H), 1455 (benzyl), 1184, 1133, 1116, 1090, 1049, and 854 (C–O–C), 736 and 698 cm^{-1} (aromatic). ^{1}H-N.m.r. data: δ 7.32 (bs, 5 H, CH_2Ph), 4.65 and 4.53 (2 d, 2 H, *J* 11 Hz, CH_2Ph), 3.80 (dd, 1 H, $J_{4,5e}$ 5.2, $J_{4,5a}$ 11.6 Hz, H-4), 3.54 (dm, 1 H, H-8*e*), 3.48 (d, 1 H, $J_{2a,2e}$ 11 Hz, H-2*a*), 3.30 (d, 1 H, H-2*e*), 3.23 (t, 1 H, $J_{8a,8e} = J_{8a,9}$ = 9 Hz, H-8*a*), 2.10 (s, 1 H, HO-3), 2.08 (dd, 1 H, $J_{4,5e}$ 5.2, $J_{5a,5e}$ 13 Hz, H-5*e*), 1.74–1.33 (m, 5 H, H-9,10*a*,10*e*,11*a*,11*e*), 1.43 (dd, 1 H, H-5*a*), 1.30 (s, 3 H, H-12,12,12), 1.23–1.06 (m, 2 H, CH_2CH_3), and 0.87 (t, 3 H, *J* 7.4 Hz, CH_2CH_3). For the ^{13}C-n.m.r. data, see Table II.

Eluted second was (3*R*,4*S*,6*R*,9*R*)-4-benzyloxy-9-ethyl-3-hydroxymethyl-1,7-dioxaspiro[5.5]undecane (**20**; 320 mg, 58%), as a colourless syrup, $[\alpha]_D$ −85° (*c* 1); ν_{max}^{film} 3462 (OH), 2067 and 3035 (C–H, aromatic), 2963, 2935, and 2878 (C–H), 1455 (benzyl), 1184, 1098, 1074, 1049, 994 (C–O–C), 736 and 698 cm^{-1} (aromatic). ^{1}H-N.m.r. data: δ 7.30 (bs, 5 H, CH_2Ph), 4.55 (s, 2 H, CH_2Ph), 4.21–4.08 (m, 2 H, H-4,12), 3.78–3.60 (m, 3 H, H-2*a*,2*e*,12'), 3.51 (dm, 1 H, H-8*e*), 3.18 (t, 1 H, $J_{8a,8e} = J_{8a,9}$ = 11 Hz, H-8*a*), 2.70 (bd, 1 H, HO-12), 2.28–2.18 (m, 1 H, H-3), 1.99 (dd, 1 H, $J_{4,5e}$ 5, $J_{5a,5e}$ 13 Hz, H-5*e*), 1.68 (t, 1

H, $J_{4,5a}$ 13 Hz, H-5*a*), 1.76–1.32 (m, 5 H, H-9,10*a*,10*e*,11*a*,11*e*), 1.13 (m, 2 H, CH_2CH_3), and 0.86 (t, 3 H, *J* 7.4 Hz, CH_2CH_3). For the ^{13}C-n.m.r. data, see Table II. Mass spectrum: *m/z* 321 [0.2%, $(M^+ + 1)$], 320 (1.2, M^+), 220 (2.4), 214 (7.2), 205 (9.1), 196 (8.1), 155 (4.5), 129 (21, $C_7H_{13}O_2^+$), 126 (20.6), 111 (12.2), 91 (100, $C_7H_7^+$), and 55 (10.5).

*(3*R*,4*S*,6*R*,9*R*)-9-Ethyl-4-hydroxy-3-hydroxymethyl-1,7-dioxaspiro[5.5]undecane [(−)-talaromycin A]* (**1**). — A solution of **20** (260 mg, 0.81 mmol) in anhydrous methanol (5 mL) that contained palladium oxide (220 mg, washed with methanol and a few drops of triethylamine) was hydrogenated overnight at 1.5 atm. T.l.c. (ether) then revealed a compound of lower mobility. The catalyst was collected and washed with methanol, and the filtrate was concentrated. Chromatography (ether → ether–methanol, 10:1) of the residue gave **1** (185 mg, quantitative), $[\alpha]_D$ −125° (*c* 0.5); lit.[4] $[\alpha]_D$ −146°; lit.[6] $[\alpha]_D$ −105.7°. The i.r. and ^{1}H-n.m.r. spectra were identical to those reported by Lynn *et al.*[1]. For the ^{13}C-n.m.r. data, see Table II. C.i.-mass spectrum (CH_4): *m/z* 231 [60%, $(M^+ + H)$], 213 [100, $(M^+ + H - H_2O)$], 183 [18, $(M^+ + H - H_2O - CH_2O)$], 165 (1), 129 (9, $C_7H_{13}O_2^+$), 79 (9), and 57 (3).

*(3*S*,4*S*,6*R*,9*R*)-9-Ethyl-4-hydroxy-3-hydroxymethyl-1,7-dioxaspiro[5.5]undecane [(−)-talaromycin B]* (**2**). — A solution of **1** (50 mg, 0.23 mmol) in anhydrous methanol (1 mL) was stirred with Amberlite IR-120 (H^+) resin (30 mg) overnight. The resin was collected and washed with methanol, and the combined filtrate and washings were concentrated. Chromatography (ether → ether–methanol, 10:1) of the residue gave **2** (48 mg, 92%), $[\alpha]_D$ −101° (*c* 0.49); lit.[4] $[\alpha]_D$ −89.1°. The i.r. and ^{1}H-n.m.r. spectra were identical to those reported by Lynn *et al.*[1]. For the ^{13}C-n.m.r. data, see Table II. C.i.-mass spectrum (CH_4): *m/z* 231 [57%, $(M^+ + H)$], 213 (100, $(M^+ + H - H_2)$], 183 [64, $(M^+ + H - H_2O - CH_2O)$], 165 (9), 129 (13, $C_7H_{13}O_2^+$), 85 (1), and 67 (1).

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