Phytochemistry, Vol. 33, No. 2, pp. 417–421, 1993
Printed in Great Britain.

0031-9422/93 $6.00+0.00

SERRULATANE DITERPENES FROM *EREMOPHILA DUTTONII*

LINDA M. TIPPETT and RALPH A. MASSY-WESTROPP*

Department of Organic Chemistry, University of Adelaide, GPO Box 498, Adelaide, South Australia, Australia

(*Received* 21 *September* 1992)

Key Word Index—*Eremophila duttonii*; Myoporaceae; diterpene; serrulatane.

Abstract—Two serrulatane diterpenes have been isolated from *Eremophila duttonii*. The structure of (3*R*)-serrulat-14-ene-3,7,8,20-tetraol, a compound suitable for conversion into the *seco*-pseudopterosins, was established on the basis of spectroscopic and chemical evidence. Further data are provided for serrulat-14-ene-7,8,20-triol and its derivatives.

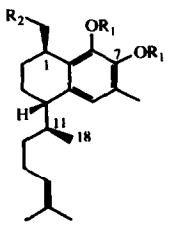
INTRODUCTION

Several papers have appeared recently describing the structures of bicyclic diterpenoids of the serrulatane class which have been isolated mainly from the genus *Eremophila* [1–3]. They also include the *seco*-pseudopterosins [4], with stereochemistry different from that of the serrulatane group, and their cyclized products, the pseudopterosins [5]. Both the *seco*-pseudopterosins and the pseudopterosins are of marine origin and occur as pentose glycosides which have been reported to be potent anti-inflammatory and analgesic agents [4, 5]. In this paper, we report the structure of a tetraol (**5a**) of the serrulatane type, together with some further data on the known triol (**1a**) and its derivatives, isolated from *Eremophila duttonii*. *Eremophila* is an Australian genus of predominantly dry area shrubs of which there are over 200 species.

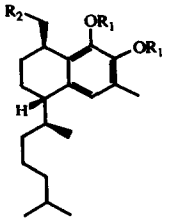
RESULTS AND DISCUSSION

The leaves of *E. duttonii* have a waxy coating which was collected by allowing the leaves to stand in ethyl ether for a short time. Because oxidation was a problem during chromatography, the crude extract was acetylated to prevent formation of quinonoid products. Chromatography then yielded the triacetate **1b** and the tetraacetate **5b**.

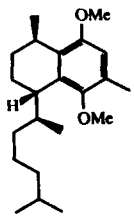
The triacetate, $C_{26}H_{36}O_6$, from microanalytical and high resolution mass spectral data, had a ^{1}H NMR spectrum consistent with **1b**. Irradiation of the H-20 protons ($-CH_2OAc$) in **1b** collapsed the signal at δ3.10, thereby establishing it as H-1. This leads to an unambiguous assignment of the resonances at δ3.10 and 2.52 to H-1 and H-4, respectively. However, because the literature assignments [1] of the corresponding signals in the parent triol **1a** are reversed and decoupling experiments were alluded to in the text, **1b** was converted into the dimethyl ether **1c** to allow a further comparison of physical data, including rotation. Reduction with $LiAlH_4$ followed by methylation with NaH and MeI in DMSO gave **1c**. Again, the ^{1}H NMR values were similar to those reported [1] for this compound, providing that the assignments of H-1 and H-4 are interchanged. However, the optical rotation, $[\alpha]_D^{23}+15.5°$ ($CHCl_3$; *c* 1.4), meas-



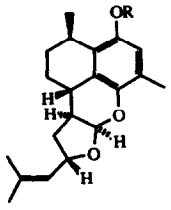
1a R_1 = H, R_2 = OH
1b R_1 = Ac, R_2 = OAc
1c R_1 = Me, R_2 = OH



2a R_1 = Me, R_2 = H
2b R_1 = Me, R_2 = OH
2c R_1 = Ac, R_2 = OAc
2d R_1 = H, R_2 = OH
2e R_1 = Me, R_2 = OTs
2f R_1 = Me, R_2 = OAc



3



4a R = H
4b R = Me

*Author to whom correspondence should be addressed.

ured on our material of high purity by 300 MHz ^{1}H NMR, was significantly different from that reported, $[\alpha]_D + 5.6°$ ($CHCl_3$; *c* 1.4). Therefore, a further derivative, the methylated dihydro deoxy compound (**2a**), which has also been described [1], was prepared. Compound **1b** was hydrogenated in the presence of Pt to give **2c**, which was reduced with $LiAlH_4$ to the triol **2d**. Methylation with two equivalents of NaH and an excess of MeI gave the dimethyl ether **2b**. Tosylation of **2b**, followed by reduction of the tosylate **2e** with $LiAlH_4$ gave **2a**. The ^{1}H NMR values of **2a** were in good agreement with the published data, except for reversal of integration for the resonances at δ0.81 and 0.93. There was only fair agreement in the rotation values: $[\alpha]_D^{23} - 10.0°$ ($CHCl_3$; *c* 0.2) and $[\alpha]_D - 18.3°$ ($CHCl_3$; *c* 1.4) [1].

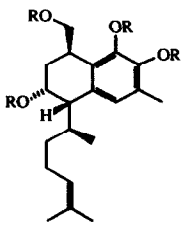
It should be noted that the chemical shift of the H-18 methyl resonance at δ0.93 for **2a** excludes the compound being epimeric at C-11. In that case, with the same 1,4-*trans*-stereochemistry, a significant upfield shift for the methyl is observed (δ0.71) [4]. The 1,4-*trans*-configuration of **1a** has been confirmed by chemical methods and will be reported elsewhere.

Compounds with the 5,8-dioxygenated pattern are also known [2, 6] in the *Eremophila* genus, but structure **3** could be excluded for **2a** as it had been prepared [7] from serrulatenol (**4a**), a compound whose structure has been established by X-ray crystal analysis [2]. The downfield shift of H-4 from δ2.52 in **2a** to δ2.80 in **3** caused by the methoxyl group at C-5, together with the chemical shift differences of the aromatic protons, δ6.50 in **3** and δ6.71 in **2a** exclude the 5,8-dihydroxy pattern for **1a**.

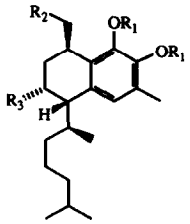
Further evidence which confirms the 7,8-dioxygenated pattern in **1a** was obtained from NOE experiments on **1c**. Irradiation of the aromatic proton at δ6.76 resulted in the strong enhancement of both the benzylic proton (H-4) at δ2.54 and aromatic methyl group at δ2.22. In the reverse experiment, irradiation of H-4 at δ2.54 resulted in the enhancement of the aromatic proton at δ6.76. It is therefore concluded that **1a** has the same structure as the compound isolated from *E. linearis* Chinnock [1], although the reasons for the rotation differences mentioned are not clear.

It is difficult to assign the relative stereochemistry with any certainty in the serrulatane series on the basis of NMR data. The only rigorous assignments of configuration have been based on X-ray crystallographic analysis, or by interrelation of a new structure with one already established from X-ray data. Therefore, the stereochemistry of **5a** at C-1, C-4 and C-11 was determined by correlation with **1a**; that of the hydroxyl group was then deduced from the coupling constants.

HR mass spectrometry established the molecular formula of **5b** as $C_{28}H_{38}O_8$. The ^{1}H NMR spectrum showed acetate methyl resonances at δ2.06 (superimposed phenolic acetates), 2.28 and 2.36, which were confirmed by absorptions in the IR spectrum at 1760, 1730 cm^{-1}. The ^{1}H NMR spectrum also showed resonances for a secondary methyl (δ0.61), two vinylic methyls (δ1.62 and 1.70), an aromatic methyl (δ2.15), an acetoxymethyl as an ABX system, δ3.76 and 4.52, a vinylic proton (δ5.12) and



5a R = H
5b R = Ac



6a R_1 = H, R_2 = R_3 = OH
6b R_1 = Ac, R_2 = R_3 = OAc
6c R_1 = Me, R_2 = R_3 = OH
6d R_1 = Me, R_2 = OTs, R_3 = OH
6e R_1 = Me, R_2 = I, R_3 = OH
6f R_1 = Me, R_2 = H, R_3 = OH
6g R_1 = Me, R_2 = H, R_3 = OCS_2Me

one aromatic proton (δ6.66). The benzylic protons appeared at δ3.07 and 3.28, with the latter being coupled to the protons of the acetoxymethyl group. Decoupling experiments showed that H-3 was coupled to the benzylic proton at δ3.07, thereby establishing the position of the secondary hydroxyl group in **5a**. Compound **2a** was chosen as a suitable target for comparison of the basic skeletons of **1a** and **5a**.

Compound **5b** was hydrogenated to **6b**, which was reduced to **6a** with $LiAlH_4$ and methylated to give the analogous dimethyl ether **6c**. However, the tosylate **6d**, formed from reaction of the primary hydroxyl group with one equivalent of TsCl in pyridine, could not be reduced satisfactorily with $LiAlH_4$ or $LiEt_3BH$. The formation of the primary tosylate was confirmed by the appearance of the nonequivalent H-20 methylene protons downfield, relative to the diol **6c**, as a doublet of the doublets at δ3.84 and 4.31. Therefore, the iodide **6e**, in which the H-20 protons appeared at δ3.17 and 3.64, was prepared from **6d** with NaI in acetone. Tri-*n*-butylstannane reduction of **6e** produced the dehalogenated compound **6f** whose structure was confirmed by the appearance of the C-1 methyl doublet at δ1.26.

The deoxygenation of the secondary hydroxyl at C-3 in **6f** was achieved by the tri-*n*-butylstannane reduction of the dithiocarbonate ester **6g** [8]. The product, 7,8-dimethoxyserrulatane (**2a**), had spectral data identical to those of the same compound obtained from **1a** and a

similar rotation, $[\alpha]_D^{22} -8.2°$ ($CHCl_3$; *c* 0.3). Therefore, **1a** and **5a** are identical, except for the additional hydroxyl group at C-3 in **5a**.

It can be deduced that the relative configuration of the two substituents at C-3 and C-4 is *cis* from an analysis of the coupling constants of the ring protons in **6f**. The couplings observed for H-3 are $J_{3,4}=4.5$ Hz, $J_{2,3}=2.8$ Hz and $J_{2,3}=11.0$ Hz. These coupling constants are consistent with a preferred conformation in which the *trans*-1,4 groups are pseudoaxial to reduce the peri-interactions and the C-3 hydroxyl group is equatorial.

Methods for the conversion of **5a** into *seco*-pseudopterosin and its isomers are currently being investigated.

EXPERIMENTAL

General. ^{1}H NMR: 60 and 300 MHz with TMS as int. standard, MS were performed at 70 eV, flash chromatography: silica gel 60 (Merck), prep. TLC: silica gel HF_{254} (Merck), bp refers to temp. of heated block.

Plant material. Eremophila duttonii was collected on the plain east of Blinman in South Australia and identification was confirmed by the Botanic Gardens, Adelaide. Specimens have been retained.

Isolation of diterpenes from Eremophila duttonii. The fresh leaves of *E. duttonii* (air-dried 2 days) were covered with Et_2O and allowed to stand for 20 min. The soln was decanted and the extraction was repeated. The Et_2O extracts were washed with satd $NaHCO_3$ soln (acidification gave only a small amount of coloured material which was discarded), washed with H_2O, dried (Na_2SO_4) and the solvent removed to yield the crude extract (4%, based on fresh leaves). Because highly coloured fractions were obtained from silica gel CC the crude extract was acetylated with Ac_2O–pyridine to prevent oxidation. Silica gel CC, then gave **1b** and the more polar **5b** (each approx. 20% of the crude acetate mixt.).

Distillation of the triacetate gave pure 8,20-diacetoxyserrulat-14-en-7-yl acetate (**1b**), bp 170–175°/0.05 mm (Found: C, 57.2; H, 6.3. $C_{26}H_{36}O_6$ requires: C, 57.1; H, 6.4%). HRMS *m/z* 444.2518. $C_{26}H_{36}O_6$ requires 444.2512. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 2950, 2900, 1760, 1730, 1450, 1370, 1170, 910. ^{1}H NMR (300 MHz, $CDCl_3$); δ0.97 (3H, *d*, $J=5.8$ Hz, H-18), 1.55, 1.65 (each 3H, *s*, H-16, H-17), 2.05 (3H, *s*, 20-OAc), 2.15 (3H, *s*, H-19), 2.28, 2.37 (each 3H, *s*, 2 × Ac), 0.9–2.4 (methylene envelope), 2.52 (1H, *m*, H-4), 3.10 (1H, *m*, H-1), 3.8 (1H, *t*, $J=6.8$ Hz, H-14), 6.95 (1H, *s*, H-5). ^{13}C NMR (75 MHz, $CDCl_3$); δ16.2, 17.6, 18.6, 18.9, 20.3, 20.5, 20.8, 21.0, 25.7, 26.2, 32.4, 33.0, 37.7, 41.7, 65.2, 124.6, 127.7, 128.7, 131.5, 139.2, 139.4, 140.9, 168.8, 170.8. EIMS *m/z* (rel. int.): 444 $[M]^+$, 231 (100).

Distillation of the tetraacetate fr. gave pure (3*R*)-7,8,20-triacetoxyserrulat-14-en-3-yl acetate (**5b**), bp 230–235°/0.01 mm. HRMS *m/z* 502.2599. $C_{18}H_{38}O_8$ requires 502.2567. IR ν_{max}^{film} cm^{-1}: 2950, 2900, 1770, 1730, 1365, 1225, 1205, 1030, 750. ^{1}H NMR (300 MHz, $CDCl_3$); δ0.61 (3H, *d*, $J=6.9$ Hz, H-18), 1.62, 1.70 (each 3H, *s*, H-16, H-17), 2.06 (6H, *s*, 2 × Ac), 2.15 (3H, *s*, H-19), 2.28, 2.36 (each 3H, *s*, 2 × Ac), 0.59–2.36 (methylene envelope), 3.07 (1H, *m*, H-4), 3.28 (1H, *m*, H-1), 3.76 (1H, *t*, $J=10.6$ Hz, H-20), 4.52 (1H, *dd*, $J=10.7$, 3.7 Hz, H-20), 5.12 (1H, *t*, $J=5.6$ Hz, H-14), 5.33 (1H, *m*, H-3), 6.66 (1H, *s*, H-5). EIMS *m/z* (rel. int.): 502 $[M]^+$, 247 (100).

Conversion of triacetate **1b** *into dimethoxy alcohol* **1c**. Compound **1b** (410 mg, 0.92 mmol) in dry Et_2O (10 ml) was reduced with a soln of $LiAlH_4$ (88 mg, 2.31 mmol) in Et_2O (10 ml) for 2 hr. H_2O (5 ml) was added carefully and the mixt. was acidified with conc. HCl to pH 1. The Et_2O layer, after drying and evapn gave **1a** (250 mg, 0.78 mmol) which was dissolved in dry DMSO and added to NaH (48 mg, 2.0 mmol, 80% in mineral oil) under N_2. After stirring for 15 min, MeI (0.29 ml, 4.72 mmol) was injected and the mixt. stirred for 18 hr. The DMSO was removed under red. pres., HCl (10%, 10 ml) was added and the mixt. extracted 2 × with CH_2Cl_2. After drying and evapn of solvent, the product was sepd by silica gel flash chromatography (solv. EtOAc–hexane, 1:4) to yield, 7,8-dimethoxyserrulat-14-en-20-ol (**1c**, 84 mg, 34%). $[\alpha]_D^{22}+15.5°$ ($CHCl_3$; *c* 1.4) (ref. [1] assigns $[\alpha]_D+5.6°$ ($CHCl_3$; *c* 1.4). ^{1}H NMR (300 MHz, $CDCl_3$); δ0.98 (3H, *d*, $J=6.8$ Hz, H-18), 1.55, 1.66 (each 3H, *s*, H-16, H-17), 2.22 (3H, *s*, H-19), 2.54 (1H, *m*, H-4), 2.61 (1H, *brs*, OH), 3.21 (1H, *m*, H-1), 3.55 (1H, *dd*, $J=7.5$, 10.3 Hz, H-20), 3.68 (1H, *dd*, $J=6.0$, 10.3 Hz, H-20), 3.80, 3.87 (each 3H, *s*, 2 × OMe), 5.00 (1H, *t*, $J=6.6$ Hz, H-14), 6.76 (1H, *s*, H-5). (Ref. [1] assignments: δ2.61, H-1; 3.23, H-4; other data in agreement.) NOEDS experiments: irradiation at δ6.76 (H-5) gave enhancement of resonances at δ2.22 (H-19, 4%) and δ2.54 (H-4, 3%). In the reverse experiment, irradiation at δ2.54 (H-4) enhanced δ6.76 (H-5, 4%).

Reduction and methylation of the triacetate **1b** *to give the dimethyl ether* **2b**. Compound **1b** (13.2 g) was hydrogenated in EtOAc (200 ml) in the presence of PtO_2 (400 mg) at room temp. for 48 hr. The reaction mixt. was filtered through Celite and the filtrate was concd under red. pres. to give **2c** (12.96 g, 98%). Distillation of a portion gave a pure sample of 8,20-diacetoxyserrulatan-7-yl-acetate (**2c**, 100 mg, 59%), bp 165–168°/0.02 mm. (Found: C, 69.7; H, 8.5. $C_{26}H_{38}O_6$ requires: C, 69.9; H, 8.6%.) IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3000, 2900, 1770, 1740, 1380, 1250, 1190, 1065. ^{1}H NMR (300 MHz, $CDCl_3$); δ0.63 (6H, *d*, $J=6.7$ Hz, H-16, H-17), 0.96 (3H, *d*, $J=6.8$ Hz, H-18), 2.05 (3H, *s*, 20-OAc), 2.11 (3H, *s*, H-19), 2.28, 2.36 (each 3H, *s*, 2 × Ac), 0.76–2.36 (methylene envelope), 2.59 (1H, *m*, H-4), 3.15 (1H, *m*, H-1), 3.8 (1H, *t*, $J=10.7$ Hz, H-20), 4.32 (1H, *dd*, $J=10.7$, 4.5 Hz, H-20), 6.97 (1H, *s*, H-5). ^{13}C NMR (75 MHz, $CDCl_3$); δ16.2, 18.8, 20.3, 20.7, 20.9, 22.5, 22.7, 25.5, 27.8, 29.6, 32.4, 33.3, 38.5, 39.1, 41.8, 65.2, 127.8, 129.0, 129.5, 139.4, 139.7, 141.1, 168.1, 168.8, 171.0. Reduction of the triacetate with $LiAlH_4$ (2.21 g) in dry THF (100 ml) gave serrulatane-7,8,20-triol (**2d**, 93%). Compound **2d** (8.6 g, 27 mmol) was methylated as described above with NaH (1.69 g, 67 mmol, as 80% slurry in mineral oil) and MeI (10.1 ml, 162 mmol) in dry DMSO (50 ml). Isolation and silica gel CC (solv. petrol–EtOAc gradient) yielded 7,8-dimethoxyserrulatan-20-ol (**2b**, 5.05 g, 54%). HRMS *m/z* 348.2674. $C_{22}H_{36}O_3$

requires 348.2664. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3460, 2928, 1482, 1402, 1368, 1316, 1266, 1104, 1070, 1012. ^1H NMR (300 MHz, $CDCl_3$); δ0.82 (6H, *d*, *J* = 6.6 Hz, H-16, H-17), 0.95 (3H, *d*, *J* = 6.8 Hz, H-18), 1.0–2.0 (methylene envelope), 2.23 (3H, *s*, H-19), 2.39 (1H, *br s*, OH), 2.53 (1H, *m*, H-4), 3.19 (1H, *m*, H-1), 3.57 (1H, *dd*, *J* = 10.2, 7.5 Hz, H-20), 3.70 (1H, *dd*, *J* = 10.2, 6.1 Hz, H-20), 3.80, 3.87 (each 3H, *s*, 2 × OMe), 6.76 (1H, *s*, H-5). EIMS *m/z* (rel. int.): 348 $[M]^+$ (11), 235 (80), 217 (100). The acetate was made for further characterization and purification with Ac_2O and Et_3N for 40 hr. Purification by prep. TLC (silica gel, solv. EtOAc–petrol, 1:4) followed by distillation yielded 7,8-dimethoxyserrulatan-20-yl acetate (**2f**), bp 198–201°/0.01 mm. (Found: C, 73.6; H, 9.9. $C_{24}H_{38}O_4$ requires: C, 73.8; H, 9.8%.) IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 2950, 1730, 1480, 1410, 1360, 1260, 1240, 1080, 1040 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$); δ0.81 (6H, *d*, *J* = 6.6 Hz, H-16, H-17), 0.94 (3H, *d*, *J* = 6.8 Hz, H-18), 1.06–2.00 (methylene envelope), 2.07 (3H, *s*, Ac), 2.22 (3H, *s*, H-19), 2.52 (3H, *m*, H-4), 3.34 (3H, *m*, H-1), 3.78, 3.88 (each 3H, s, 2 × OMe), 4.00 (1H, *dd*, A part of an ABX, *J* = 10.3, 10.6 Hz, H-20), 4.17 (1H, *dd*, B part of ABX, *J* = 10.6, 4.2 Hz, H-20), 6.72 (1H, *s*, H-5). EIMS *m/z* (rel. int.): 390 $[M]^+$ (38), 330 (36), 217 (100). Hydrolysis of **2f** with NaOH in MeOH gave pure **2b**.

A crystalline derivative, but unsuitable for X-ray analysis, of the alcohol **2b** (300 mg) was prepared with anthraquinone-2-carbonyl chloride (235 mg) and 4-*N*, *N*-dimethylaminopyridine (5 mg) in pyridine (2 ml) at 55° for 2 days. Isolation and silica gel flash chromatography (solv. EtOAc–hexane, 3:17) followed by recrystallization (hexane) gave 7,8-dimethoxyserrulatan-20-yl anthraquinone-2-carboxylate (245 mg, 49%) as a yellow solid, mp 61–63°. HRMS *m/z* 582.3001. $C_{37}H_{42}O_6$ requires 582.2981. ^1H NMR (300 MHz, $CDCl_3$); δ0.83 (6H, *d*, *J* = 6.7 Hz, H-16, H-17), 0.97 (3H, *d*, *J* = 6.9 Hz, H-18), 1.00–2.00 (methylene envelope), 2.24 (3H, *s*, H-19), 2.60 (1H, *m*, H-4), 3.56 (1H, *m*, H-1), 3.79, 3.93 (each 3H, *s*, 2 × OMe), 4.33 (1H, *t*, A part of an ABX, *J* = 10.4 Hz, H-20), 4.53 (1H, *dd*, B part of an ABX, *J* = 10.4, 4.3 Hz, H-20), 7.26 (1H, *s*, H-5), 7.8 (2H, *m*, H-6′, H-7′), 8.4 (4H, *brm*, H-3′, H-4′, H-5′, H-8′), 8.98 (1H, *d*, *J* = 1.6 Hz, H-1′). EIMS *m/z* (rel. int.): 582 $[M]^+$ (100).

Tosylation of **2b** *and its reduction to* **2a**. The purified alcohol **2b** (385 mg) was tosylated with TsCl (212 mg) in pyridine (1 ml). Work-up and purification by prep. TLC (solv. EtOAc–petrol, 1:9) yielded, as an oil, 7,8-dimethoxyserrulatan-20-yl tosylate (**2e**, 368 mg, 66%). HRMS *m/z* 502.2774. $C_{29}H_{42}O_5S$ requires 502.2753. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 2932, 1712, 1600, 1462, 1408, 1360, 1176, 1098, 1072, 948. ^1H NMR (300 MHz, $CDCl_3$); δ0.81 (6H, *d*, *J* = 6.6 Hz, H-16, H-17), 0.90 (3H, *d*, H-18), 1.0–1.90 (methylene envelope), 2.20 (3H, *s*, H-19), 2.44 (3H, *s*, Me-Ar), 3.30 (1H, *m*, H-1), 3.73, 3.75 (each 3H, *s*, 2 × OMe), 3.81 (1H, *dd*, A part of an ABX, *J* = 9.7, 10.5 Hz, H-20), 4.21 (1H, *dd*, B part of an ABX, *J* = 9.7, 3.8 Hz, H-20), 6.69 (1H, *s*, H-5), 7.32, 7.79 (each 2H, *d*, *J* = 8.3 Hz, arom.). EIMS *m/z* (rel. int.): 502 $[M]^+$ (31), 217 (100). Compound **2e** (185 mg) was reduced with $LiAlH_4$ (56 mg) in dry THF (5 ml). Isolation and purification by prep. TLC (solv. EtOAc–petrol, 1:19) gave 7,8-dimethoxyserrulatane (**2a**, 62 mg, 50%) as an oil. HRMS *m/z*. Found: 332.2709 (calcd for $C_{22}H_{36}O_2$: 332.2715). $[\alpha]_D^{20}$ −10.0° ($CHCl_3$; *c* 0.2) [ref. [1] assigns $[\alpha]_D$ −18.3° ($CHCl_3$; *c* 1.4)]. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 2928, 2864, 1466, 1402, 1260, 1226, 1102, 1008. ^1H NMR (300 MHz, $CDCl_3$); δ0.81 (6H, *d*, *J* = 6.5 Hz, H-16, H-17), 0.93 (3H, *d*, *J* = 6.8 Hz, H-18), 1.17 (3H, *d*, *J* = 7.0 Hz, H-20), 1.2–1.9 (methylene envelope), 2.22 (3H, *s*, H-19), 2.52 (1H, *m*, H-4), 3.12 (1H, *m*, H-1), 3.80, 3.87 (each 3H, *s*, 2 × OMe), 6.71 (1H, *s*, H-5). The ^1H NMR data reported [1] are the same, except for reversal of integration at δ0.81 and 0.93. EIMS *m/z* (rel. int.): 332 $[M]^+$ (12), 217 (100).

Catalytic reduction of the tetraacetate **5b**. Compound **5b** (118 mg) was hydrogenated in the presence of PtO_2 (15 mg) and EtOAc (3 ml) for 60 min at room temp. The reaction mixt. was filtered through Celite and the filtrate evapd under red. pres. Distillation of the residue gave (3*R*)-7,8,20-triacetoxyserrulatan-3-yl acetate (**6b**, 85 mg, 72%), bp 172°/0.02 mm. HRMS *m/z* 504.2738. $C_{28}H_{40}O_8$ requires 504.2723. IR ν_{max}^{film} cm^{-1}: 2950, 2900, 1770, 1730, 1385, 1205, 1030, 755. ^1H NMR (300 MHz, $CDCl_3$); δ0.56 (3H, *d*, *J* = 6.9 Hz, H-18), 0.86 (6H, *d*, *J* = 6.3 Hz, H-16, H-17), 2.07 (6H, *s*, 2 × Ac), 2.12 (3H, *s*, H-19), 2.29, 2.36 (each 3H, *s*, 2 × Ac), 0.8–2.2 (methylene envelope), 3.07 (1H, *m*, H-4), 3.28 (1H, *m*, H-1), 3.76 (1H, *t*, *J* = 10.5 Hz, H-20), 4.52 (1H, *dd*, *J* = 10.6, 3.5 Hz, H-20), 5.33 (1H, *m*, H-3), 6.65 (1H, *s*, H-5).

Reduction of the tetraacetate **6b** *and selective methylation of the product tetraol* **6a**. Compound **6b** (2.16 g, 4.29 mmol) was reduced with $LiAlH_4$ (652 mg, 17.20 mmol) in dry THF (20 ml) as described above to yield (3*R*)-serrulatane-3,7,8,20-tetraol (**6a**, 1.34 g, 93%). Compound **6a** was methylated, using NaH (251 mg, 80% in mineral oil), DMSO (20 ml) and MeI as described above. Sepn by silica gel flash chromatography (solv. EtOAc–petrol, 7:3) gave (3*R*)-7,8-dimethoxyserrulatane-3,20-diol (**6c**, 660 mg, 48%) as an oil. HRMS *m/z* 364.2610. $C_{22}H_{36}O_4$ requires 364.2613. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3440, 3020, 2928, 1482, 1410, 1072. ^1H NMR (300 MHz, $CDCl_3$); δ0.60 (3H, *d*, *J* = 6.8 Hz, H-18), 0.89 (6H, *d*, *J* = 6.5 Hz, H-16, H-17), 1.0–2.0 (methylene envelope), 2.23 (3H, *s*, H-19), 2.75 (1H, *m*, H-4), 3.33 (1H, *m*, H-1), 3.57 (1H, *m*, H-20), 3.74 (1H, *m*, H-20), 3.80, 3.85 (each 3H, *s*, 2 × OMe), 6.68 (1H, *s*, H-5). EIMS *m/z* (rel. int.): 364 $[M]^+$ (79), 233 (97), 205 (100).

Preparation of iodo alcohol **6e** *from diol* **6c**. Tosylation of diol **6c** (290 mg) in pyridine–CCl_4 for 48 hr gave, after sepn by silica gel flash chromatography (solv. EtOAc–petrol, 1:3), 3*R*-3-hydroxy-7,8-dimethoxyserrulatan-20-yl tosylate (**6d**, 234 mg, 57%) as an oil. HRMS *m/z* 518.2667. $C_{29}H_{42}O_6S$ requires 518.2710. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3600, 2924, 2900, 1598, 1464, 1410, 1360, 1176, 960. ^1H NMR (300 MHz, $CDCl_3$); δ0.52 (3H, *d*, *J* = 6.9 Hz, H-18), 0.87 (6H, *d*, *J* = 6.7 Hz, H-16, H-17), 1.0–2.0 (methylene envelope), 1.51 (1H, *s*, OH), 2.21 (3H, *s*, H-19), 2.24 (3H, *s*, Me-Ar), 2.72 (1H, *m*, H-4), 3.43 (1H, *m*, H-1), 3.72, 3.74 (each 3H, *s*, 2 × OMe), 3.84 (1H, *dd*, *J* = 9.4, 10.2, H-20), 4.31 (1H, *dd*, *J* = 10.2, 3.7 Hz, H-20), 4.12 (1H, *m*, H-3), 6.62 (1H, *s*, H-5), 7.32, 7.77 (each 2H, *br*

d, arom.). EIMS *m/z* (rel. int.): 518 $[M]^+$ (38), 500 (100).

Compound **6d** (84 mg) was refluxed with NaI (146 mg) in dry Me_2CO (7 ml) under N_2 for 48 hr. Work-up, as described above and purification by silica gel flash chromatography (solv. EtOAc–hexane, 1:9) yielded (3*R*)-20-iodo-7,8-dimethoxyserrulatan-3-ol (**6e**, 50 mg, 65%). HRMS *m/z* 474.1613. $C_{22}H_{35}IO_3$ requires 474.1631. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3604, 2952, 1480, 1408, 1180, 1076. ^1H NMR (300 MHz, $CDCl_3$); δ0.61 (3H, *d*, $J=6.9$ Hz, H-18), 0.88 (6H, *d*, $J=7.0$ Hz, H-16, H-17), 1.0–2.2 (methylene envelope), 2.23 (3H, *s*, H-19), 2.73 (1H, *m*, H-4), 3.17 (1H, *t*, $J=9.2$ Hz, H-20), 3.64 (1H, *dd*, $J=9.2$, 2.7 Hz, H-20), 3.40 (1H, *m*, H-1), 3.79, 3.89 (each 3H, *s*, 2 × OMe), 4.25 (1H, *m*, H-3), 6.66 (1H, *s*, H-5). EIMS *m/z* (rel. int.): 474 $[M]^+$ (59), 361 (100).

*Tri-*n*-butylstannane reduction of iodo alcohol* **6e**. To the iodo compound **6e** (36 mg, 0.76 mmol) and AIBN (2 mg) in C_6H_6 (1 ml) was added tri-*n*-butylstannane (132 mg, 0.12 ml) and the mixt. refluxed overnight. After removal of C_6H_6, the residue was dissolved in Et_2O and washed with 10% KF soln. After drying and solvent removal, the tin by-products were removed by silica gel flash chromatography with petrol. Elution (solv. EtOAc–hexane, 1:9) then gave (3*R*)-7,8-dimethoxyserrulatan-3-ol (**6f**, 17 mg, 65%) as an oil. HRMS *m/z* 348.2674. $C_{22}H_{36}O_3$ requires 348.2664. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3450, 2924, 2864, 1602, 1466, 1408, 1380, 1328, 1204, 1068. ^1H NMR (300 MHz, $CDCl_3$); δ0.53 (3H, *d*, $J=6.9$ Hz, H-18), 0.88 (6H, *d*, $J=6.5$ Hz, H-16, H-17), 1.26 (3H, *d*, $J=7.0$ Hz, H-20), 1.00–1.65 (methylene envelope), 1.61 (1H, *s*, OH), 2.08 (2H, *m*, H-2α, H-11), 2.23 (3H, *s*, H-19), 2.79 (1H, *m*, H-4), 3.25 (1H, *m*, H-1), 3.79, 3.85 (each 3H, *s*, 2 × OMe), 4.31 (1H, *ddd*, $J=11$, 4.5, 2.8 Hz, H-3), 6.62 (1H, *s*, H-5). EIMS *m/z* (rel. int.): 348 $[M]^+$ (26), 235 (100).

Preparation and reduction of xanthate ester **6g**. The alcohol **6f** (20 mg), NaH (6 mg, 80% in mineral oil) and imidazole (2 mg) were refluxed in dry THF (2 ml) for 4 hr under N_2. CS_2 (0.2 ml) was added and refluxing was continued for a further 30 min. MeI (49 mg, 0.021 ml) was then added and refluxing continued for 30 min. After solvent removal the residue was dissolved in CH_2Cl_2 and washed with H_2O and satd NH_4Cl soln. It was dried, concd and purified by silica gel flash chromatography (solv. CH_2Cl_2–hexane, 1:1) to yield (3*R*)-*O*-[7,8-dimethoxyserrulatan-3-yl] *S*-methyl dithiocarbonate (**6g**, 14 mg, 56%) as an oil. ^1H NMR (300 MHz, $CDCl_3$); δ0.55 (3H, *d*, $J=7.1$ Hz, H-18), 0.87 (6H, *d*, $J=6.7$ Hz, H-16, H-17), 1.31 (3H, *d*, $J=7.0$ Hz, H-20), 1.35–2.70 (methylene envelope), 2.53 (3H, *s*, H-19), 2.76 (3H, *s*, SMe), 3.21 (1H, *m*, H-4), 3.32 (1H, *m*, H-1), 3.79, 3.86 (each 3H, *s*, 2 × OMe), 6.14 (1H, *m*, H-3), 6.59 (1H, *s*, H-5). EIMS *m/z* (rel. int.): 438 $[M]^+$ (5), 217 (100).

Tri-*n*-butylstannane (0.1 ml) was added to a hot soln of the xanthate ester (22 mg) and AIBN (2 mg) in dry C_6H_6 and the mixt. refluxed for 16 hr. Work-up and silica gel flash chromatography with petrol removed the tin by-products and further elution (solv. CH_2Cl_2–hexane, 2:3) yielded **2a** (6 mg, 35%), with spectral data identical to those obtained on **2a** derived from the triol **1a**. $[\alpha]_D^{22}$ $-8.2°$ ($CHCl_3$; *c* 0.3).

REFERENCES

1. Croft, K. D., Ghisalberti, E. L., Jefferies, P. R. and Proudfoot, G. M. (1981) *Aust. J. Chem.* **34**, 1951.
2. Abel, A. D., Horn, E., Jones, G. P., Snow, M. R., Massy-Westropp, R. A. and Riccio, R. (1985) *Aust. J. Chem.* **38**, 1837.
3. Ghisalberti, E. L., Jefferies, P. R. and Vu, H. T. N. (1990) *Phytochemistry* **29**, 316.
4. Look, S. A. and Fenical, W. (1987) *Tetrahedron* **43**, 3363.
5. Look, S. A., Fenical, W., Matsumoto, G. K. and Clardy, J. (1986) *J. Org. Chem.* **51**, 5140.
6. Abel, A. D. and Massy-Westropp, R. A. (1985) *Aust. J. Chem.* **38**, 1263.
7. Cowin, L. M. and Massy-Westropp, R. A. (1992) *J. Nat. Prod.* **55**, 1790.
8. Barton, D. H. R. and McCombie, S. W. (1975) *J. Chem. Soc. Perkin Trans I* 1574.