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SERRULATANE DITERPENES FROM *EREMOPHILA* SPP.*

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Key Word Index—*Eremophila* spp.; Myoporaceae; serrulatane diterpenes.

Abstract—Nine new serrulatane diterpenes have been isolated from various *Eremophila* species. Chemical and spectroscopic evidence for their structure is presented.

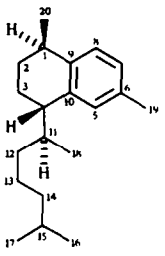
INTRODUCTION

In the course of our survey on the phytochemistry of *Eremophila* we have isolated a number of bicyclic and tricyclic diterpenes in which only three isoprenoid units are involved in the cyclization process and which can be considered as isoprenologues of cyclic sesquiterpenes [1–4]. The most common diterpene class encountered so far in *Eremophila* contains the serrulatane skeleton (**1**), an isoprenologue of the calamenene sesquiterpenes, whose structure, absolute configuration and numbering system has been defined [5] as shown in **1**. During our study numerous serrulatane metabolites have been indicated and the structures of some of these have been reported previously [5, 6]. We now wish to report further examples of this type for which we have assigned structure and stereochemistry. To facilitate presentation, species containing the same major metabolite(s) have been grouped into sub headings and some of the less pertinent transformations and data have been relegated to the Experimental section.

RESULTS AND DISCUSSION

Eremophila drummondii *var.* brevis, *S Moore and* E. woolsiana *F. Muell.*

The acidic portion of an extract of *E. drummondii* var. *brevis* appeared from TLC to contain three major components which were separated by rapid silicic acid chromatography. The most polar component was characterized as a tetrahydroxy acid (**2**) by formation of a tetraacetoxy methyl ester (**3**) on methylation with diazomethane followed by acetylation with acetic anhydride. The ^{1}H NMR spectrum of **3** included signals for an aromatic proton (δ7.29), two methyleneoxy groups (3.73–3.94, *m*), a carbomethoxyl group (3.88), two benzylic protons (3.00, *m*), two aromatic and two aliphatic acetoxy methyl groups (2.33, 2.31 and 2.06, 2.03 respectively) and two secondary methyl groups (1.17, *d*; 0.86, *d*). Treatment of compound **2** with dimethyl sulphate–potassium carbonate yielded the dimethoxy methyl ester (**4**) confirming the presence of two phenolic hydroxyl groups in the tetrahydroxy acid (**2**). The spectroscopic properties of these compounds suggested that their structure was based on a serrulatane skeleton. Evidence for this was obtained by interrelation of **2** *via* the dimethoxy methyl ester (**4**) with the known benzyl alcohol (**5**) [1]. Thus treatment of **4** with toluene-*p*-sulphonyl chloride and reduction of the



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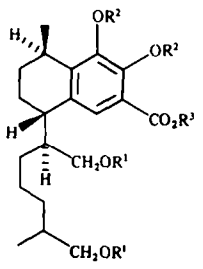
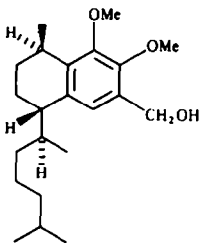


	R^1	R^2	R^3
2	H	H	H
3	Ac	Ac	Me
4	H	Me	Me



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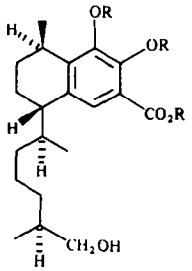
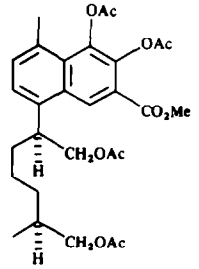


6 R = H
7 R = Me



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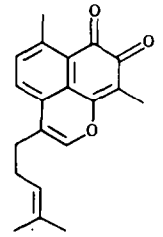

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* Part 23 in the series "The Chemistry of *Eremophila* spp." For Part 22 see *Aust. J. Chem.* (1985) **38**, 1351.

ditosylate with lithium aluminium hydride yielded a compound identical with **5**.

The presence of the two primary hydroxyl groups on the side chain in **2** was deduced from the mass spectrum of **2** and its derivatives which showed significant ions for the loss of the side chain [$C_8H_{17}O_2$ or $C_8H_{15}(OAc)_2$] arising from fragmentation of the C-4,C-11 benzylic bond. Comparison of the ^{13}C NMR spectrum of **2** with that of **7** (Table 1), a derivative of a metabolite **6** previously isolated from *E. drummondii* [5], indicated that the two primary hydroxyl groups in **2** were located at C-11 and C-15. The chemical shift of two tertiary carbon atoms in **2** were shifted with respect to those in **7**: one deshielded by ~ 8 ppm and the other shielded by 5 ppm consistent with the α- and β-effects of a hydroxyl group located at C-18.

Confirmation of this point was obtained by dehydrogenation of the tetraacetoxy ester (**3**) with DDQ to the naphthalene (**8**). The ^1H NMR spectrum of **8** lacked resonances for the two benzylic protons at C-4 and C-1 but included signals for three aromatic protons (δ8.79, 1H; 7.24, 2H) and an aromatic methyl (2.71). Irradiation for the region between δ3.66 and 3.94, which contains signals for H-11 and three of the four methyleneoxy protons, did not collapse the signal for the secondary methyl group at 0.81 thus excluding a structure with a methyl group at C-11. Compound **2** is thus shown to be 7,8,16,17-tetrahydroxyserrulatan-19-oic acid with the stereochemistry at C-15 assumed to be the same (*S*) as that determined for the trihydroxy acid (**6**) isolated [5] from the closely related *E. drummondii*.

The other two acids isolated were formulated as the 18-monoacetoxy and 16,18-diacetoxy derivatives of **2** on the basis of their spectroscopic properties. Mild hydrolysis (trimethylamine–methanol) of the diacetate afforded the monoacetate suggesting that the acetoxy group in the latter was in the more hindered position at C-18. Treatment of each with diazomethane followed by acetylation yielded the tetraacetate ester (**3**).

The serrulatane diterpenes contain the same bicarbocyclic skeleton as a biflorin (**9**), an orthoquinone isolated originally from *Capraria biflora* (Scrophulariaceae) [7] and subsequently from *E. latrobei* [Ghisalberti, E. L., Ghosh, J. and Jefferies, P. R., unpublished results]. The isolation of 18-hydroxylated serrulatanes with an *o*-quinol oxygenation pattern suggested that these may arise from precursors of biflorin and also that the heterocyclic ring system of biflorin might be accessible by chemical oxidation of the tetrahydroxy acid (**2**). In the event treatment of the methyl ester derivative of **2** with Fremy's salt yielded an *o*-quinone [ν_{max} 1 670 cm^{-1}; λ_{max}^{EtOH} nm (log ε): 234 (4.44), 255 (4.43), 289 (4.34), 450 (3.68)] which lacked ^1H NMR resonances for aromatic protons. Reductive acetylation of this quinone afforded the crystalline triacetate ether (**10**) whose spectroscopic properties are consistent with the structure assigned.

In particular the ^1H NMR spectrum of **10** lacked signals for aromatic protons and showed signals at δ2.27 and 2.22 for two aromatic acetate groups (ν_{max} 1795 and 1785 cm^{-1}) and at 2.06 (ν_{max} 1750 cm^{-1}) for one aliphatic acetate. In addition the ^{13}C NMR spectrum (Table 1) showed six singlets for the aromatic carbons, three of which (δ153.0, 152.4 and 142.6) carry an oxygen functionality. Presumably in this reaction the C-18 hydroxyl group undergoes an intramolecular β-addition with an

Table 1. ^{13}C NMR Chemical shifts of selected serrulatanes*

Carbon	2†	7	10	11	12	16	17‡	18‡	22	23
1	28.4	27.2	28.5	35.7	32.8	27.6	41.5	41.5	35.6	32.7
2	28.9	27.9	30.1	23.3	21.0	26.6§	69.4	69.0	22.8	20.7
3	20.1	19.4	24.2	20.5	19.0	19.7	30.5	30.6	19.9	18.8
4	36.8	42.0	37.7	42.5	42.2	42.6	47.2	46.5	42.4	42.1
5	120.7	122.5	153.0	123.7	128.6	122.5	117.7	116.6	122.5	128.2
6	110.5	126.4	114.7	127.8	128.2	128.9	121.1	134.4	128.1	128.9
7	147.7	150.6	152.4	114.6	121.6	108.6	141.5	113.6	114.6	121.3
8	143.4	151.7	142.6	155.3	149.4	157.4	143.6	155.4	155.5	149.4
9	131.5	142.5	142.6	132.2	135.2	134.8	124.0	122.3	132.0	134.1
10	137.6	135.9	130.7	142.5	143.5	140.7	130.9	141.9	141.8	143.0
11	46.8	38.5	37.0	37.7	37.9	38.5	31.6	31.5	38.2	38.5
12	28.1	33.4	30.3	33.2	33.1	33.8	32.1	31.9	27.0	27.2
13	26.1	25.2	26.8	26.3	26.1	25.6§	25.8	25.7	39.0	38.6
14	34.3	33.6	33.8	124.9	124.5	39.3	124.7	124.7	216.1	214.7
15	36.3	35.8	32.5	131.6	131.8	27.9	130.9	130.8	40.8	40.8
16	67.9	68.2	69.3	25.7	25.6	22.5‖	25.5	25.4	18.2	18.3
17	17.1	16.6	16.9	17.7	17.7	22.8‖	17.4	17.3	18.2	18.3
18	63.7	18.9	70.3	18.7	18.6	18.9	18.0	18.0	18.7	18.8
19	173.4	167.0	169.3	171.7	171.4	21.6‖	16.2	20.9	167.9	166.5
20	21.2	22.2	20.9	67.9	65.3	21.6‖	65.0	63.4	67.6	65.1

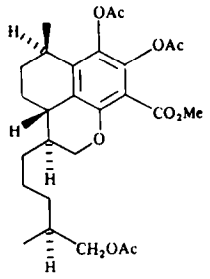
Other signals. **7**, OMe (52.6, 60.7, 61.2); **10**, OMe (52.5), OAc (20.6, 20.9, 21.0, 171.3, 171.3, 171.7); **12**, OAc (21.0, 21.0, 169.7, 171.1); **22**, OMe (52.1); **23**, OMe (52.2), OAc (21.1, 21.1, 169.6, 170.6).

*Multiplicity of signals were determined by SFORD and GASPE techniques and are consistent with assignments. $CDCl_3$ as solvent unless otherwise mentioned.

†Acetone-d_6.

‡DMSO-d_6.

§‖Values may be interchanged.



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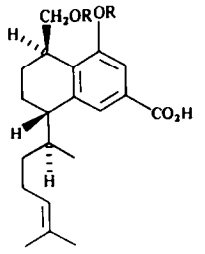
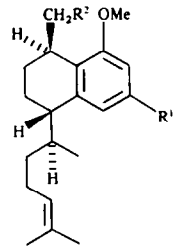
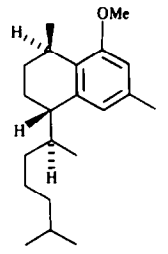


11 R = H
12 R = Ac



	R^1	R^2
13	CO_2Me	OH
14	CO_2Me	OTs
15	CH_2OH	H



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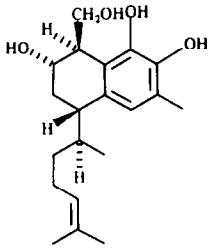

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acid. The dihydroxy acid (**11**) was found also to be the major acid in extracts of *E. denticulata* and the northern race of *E. decipiens*.

Eremophila hughesii *F. Muell. and* E. gibsonii *F. Muell.*

The main acidic component isolated from *E. hughesii* was a tetraol which was shown to be identical with (2*S*)-serrulat-14-ene-2,7,8,20-tetraol (**17**) previously [5] isolated from *E. granitica*. Also isolated was the diacetoxy acid (**12**).

The sodium hydroxide soluble portion of an extract from *E. gibsonii* on fractionation yielded two major components which were shown to be the tetraol (**17**) and a new triol (**18**) which was characterized as the methyl ether (**19**) and the ethylidene derivative (**20**). The ^{1}H NMR spectral properties were consistent with the structure proposed and comparison of the ^{13}C NMR spectra of **18** and **17** (Table 1) showed that the former lacked one hydroxyl group on the aromatic ring (δ116.6, *d*, C-5; δ113.6, *d*, C-7). Apart from the resonances assigned to the sp^2-hybridized carbons of the aromatic ring a good correspondence was observed between the chemical shifts of the remaining carbon atoms and thus the structure of **18** is indicated as (2*S*)-serrulat-14-ene-2,8,20-triol.

Eremophila virens *C. A. Gardn*

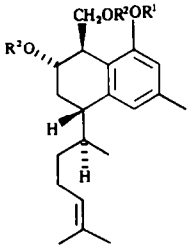
The major acidic metabolite isolated was identical with the dihydroxy acid **11** previously obtained from *E. glabra*. Chromatography of a portion of the extract soluble in sodium hydroxide solution yielded a dihydroxy acid (**21**) ($\nu_{max}^{CCl_4}$ 3640, 1730 cm^{-1}) which was characterized as the dihydroxy ester (**22**) and the diacetoxy methyl ester (**23**). The ^{1}H NMR spectrum of **23** included signals for

intermediate *o*-quinone. Intermolecular variants of this reaction are known [8]. Careful screening of the sodium hydroxide soluble portion of the plant extract afforded small quantities of an unstable compound which after acetylation and methylation gave a triacetate methyl ester identical with **10**.

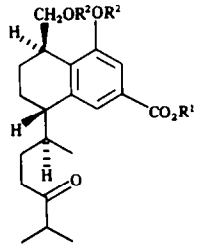
The acidic components of *E. woolsiana* were shown to be identical with the three major acids isolated from *E. drummondii* var. *brevis* as described above.

Eremophila glabra (*R. Br.*) *Ostenf.*, E. denticulata *F. Muell. and* E. decipiens *Ostenf.*

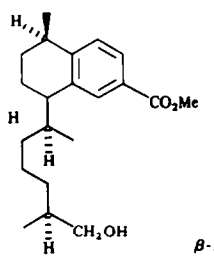
The major acidic components of *E. glabra* were shown to be 8,20-dihydroxyserrulat-15-en-19-oic acid (**11**) and the corresponding diacetate (**12**). The structures proposed for **11** and **12** could be inferred from ^{1}H NMR and mass spectral characteristics and in particular the presence of a primary hydroxyl group at C-1 in **11** rather than C-11 is evident from the mass spectrum of **11** which shows a significant ion at *m/z* 203 arising from loss of the side chain (C_8H_{15}) from the $[M-H_2O]^+$ ion (*m/z* 314). The stucture and stereochemistry of **11** and **12** were confirmed by interrelation of **11**, *via* the sequence **11** → **13** → **14** → **15**, with 8-methoxyserrulatane (**16**), previously prepared [6] from 8,17-dihydroxyserrulat-15-en-19-oic



	R^1	R^2
18	H	H
19	Me	H
20	H	Me–C(Me)–H



	R^1	R^2
21	H	H
22	Me	H
23	Me	Ac



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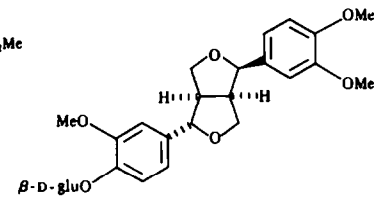

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two *meta*-oriented aromatic protons (δ 7.78 and 7.58, J_{meta} = 1.5 Hz), a carbomethoxyl group (3.88), an aromatic (2.38) and an aliphatic (2.05) acetoxymethyl group and three secondary methyl group (1.02, 6H, *d*, J = 7 Hz; 0.97, 3H, *d*, J = 7 Hz). In addition signals for a methylacetoxy group appeared as the AB part of an ABX system (δ_A 4.32, δ_B 3.82, J_{AB} = 10.5 Hz, J_{AX} = 4.5 Hz, J_{BX} = 10.5 Hz) which was shown by NMDR measurements to be coupled to a benzylic proton (δ 3.30) which in turn was coupled to methylene protons resonating at *ca* δ 1.87. The presence of a carbonyl group at C-14 was inferred from the mass spectra of **21**, **22** and **23** all of which showed significant ions at m/z 71 presumably arising from cleavage of the C-13,C-14 bond. Proof for the structure assigned was obtained by conversion of the congener **11** to **23**. Thus **11** was converted to its diacetoxy methyl ester derivative which was hydroborated and the mixture of epimeric alcohols obtained was oxidized to give a keto diacetoxy ester identical with **23**.

E. biserrata *Chinnock and* E. racemosa

The major diterpene acid isolated from this plant was purified as the methyl ester derivative which was shown to be identical to methyl (15*S*)-16-hydroxyserrulatan-19-oate (**24**) prepared previously [5].

No significant quantity of diterpene acids were isolated from *E. racemosa*. The major compound isolated was shown to be the lignan phillyrin (**25**) by comparison of its physico-chemical properties and those of its aglycone, obtained by treatment of **25** with emulsin, with those reported in the literature [9].

EXPERIMENTAL

Mps (Kofler apparatus) are uncorr. IR spectra were recorded with either Perkin–Elmer 283 or 1310 IR Spectrophotometers. ^{1}H NMR spectra were recorded with a Hitachi Perkin–Elmer R-24B Spectrometer (60 MHz), a Bruker WP-80 Spectrometer (80 MHz) or a Bruker HX-90 Spectrometer (90 MHz); ^{13}C NMR spectra were recorded using a Bruker WP-80 Spectrometer (20.1 MHz). UV spectra were obtained using a Hewlett–Packard 8450 A UV/VIS Spectrophotometer. MS were measured with either a Varian MAT CH-7 MS (65–70 eV) or a Hewlett–Packard 5986 GC/MS System (35 eV). HRMS were recorded on a Varian MAT-31 Spectrometer. $[\alpha]_D$ were measured using a Perkin–Elmer 141 Polarimeter with a 1 dm cell.

Voucher specimens of all the plants have been deposited with the Western Australian State Herbarium.

General procedure for the extraction of plant samples. Fresh leaves and terminal branches of the plant were soaked overnight in Me_2CO. The solvent was evaporated and the residue dissolved in Et_2O was washed sequentially with 8% aq. $NaHCO_3$ and 5% aq. NaOH soln. In each case the aq. fractions were acidified with 10% aq. HCl and re-extracted with Et_2O. The ethereal layers were dried ($MgSO_4$), filtered and evaporated to yield $NaHCO_3$-soluble, NaOH-soluble and neutral fractions, respectively.

Isolation of metabolites from E. drummondii *var.* brevis. A sample of the flowering plant (176 g), collected in September 1982 43 km from Corrigin to Bendering in Western Australia, yielded $NaHCO_3$-soluble (36.8 g), 5% aq. NaOH-soluble (4.19 g) and neutral (3.26 g) fractions. A portion (11.5 g) of the bicarbonate extract was chromatographed by rapid silicic acid filtration (RSF). Elution with CH_2Cl_2–EtOAc (4:1) yielded fractions of 16,18-diacetoxy-7,8-dihydroxyserrulatan-19-oic acid as an orange oil (3.21 g); IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3700, 1735, 1680; ^{1}H NMR ($CDCl_3$, 60 MHz): δ0.87 (3H *d*, J = 7 Hz, Me-17) 1.21 (3H, *d*, J = 7 Hz, Me-20), 2.03 (6H, *s*, OAc), 2.81 (1H, *m*, $W_{1/2}$ = 12 Hz, H-4), 3.21, (1H, *m*, $W_{1/2}$ = 14 Hz, H-1), 3.68–4.28 (4H, *m*, 16-H_2 and 18-H_2), 7.13 (1H, *s*, H-5); MS m/z (rel. int.): 450 $[M]^+$; (9) 432 (8), 391 (19), 372 (25), 221 (100), 203 (99), 177 (41). Elution with CH_2Cl_2–EtOAc (3:2) gave 18-acetoxy-7,8,16-trihydroxyserrulatan-19-oic acid as a pale orange foam (2.06 g); IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3700, 1730, 1670; ^{1}H NMR ($CDCl_3$; 60 MHz): δ0.85 (3H, *d*, J = 7 Hz, Me-17), 1.19 (3H, *d*, J = 7 Hz, Me-20), 2.04 (3H, *s*, OAc), 2.82 (1H, *m*, $W_{1/2}$ = 13 Hz, H-4), 3, 12 (1H, *m*, $W_{1/2}$ = 8 Hz, H-1), 3.35 (2H, AB part of ABX, 18-H_2), 3.95 (2H, AB part of ABX, 16-H_2), 7.15 (1H, *s*, H-6); MS m/z (rel. int.): 408 $[M]^+$ (10), 390 (9), 348 (9), 221 (100), 203 (99). Elution with CH_2Cl_2–EtOAc (1:4) gave 7,8,16,18-tetrahydroxyserrulatan-19-oic acid (**2**, 1.96 g) as a pale orange foam, $[\alpha]_D$ −37.2° (*c* 4; C_5H_5N); ^{1}H NMR (Me_2CO-d_6, 90 MHz): δ0.81 (3H, *d*, J = 6.5 Hz, Me-17), 1.22 (3H, *d*, J = 6.5 Hz, Me-20), 2.92–3.15 (2H, *m*, H-4 and H-1), 3.33 and 3.60 (4H, centres of AB part of ABX, 18-H_2 and 16-H_2 respectively), 7.36 (1H, *s*, H-5); ^{13}C NMR: Table 1. MS m/z (rel. int.): 366 $[M]^+$ (22), 348 (7), 330 (7), 312 (10), 221 (100), 218 (15), 203 (71). The first two compounds were methylated with CH_2N_2 and the methyl esters were treated with Ac_2O–C_5H_5N. In each case the product formed had identical spectral parameters to the sample of the tetraacetoxy methyl ester prepared from **2** as described below.

RSF chromatography of a portion (1.67 g) of the fraction soluble in NaOH on elution with CH_2Cl_2–EtOAc (1:4) gave an oil (106 mg) which was purified by TLC (EtOAc) to give a fraction (28 mg) which was methylated with CH_2N_2 and then treated with Ac_2O–pyridine to yield a triacetate ester which crystallized from $CHCl_3$–pentane as needles, mp 149–151°; $[\alpha]_D$ −11.6° (*c* 0.2; $CHCl_3$). An mmp (149–151°) and spectral parameters showed it to be identical to **10** prepared as described below.

Derivatives of the tetrahydroxy acid **2**. (a) A sample of **2** (110 mg) was treated with Ac_2O–C_5H_5N for 24 hr and the product recovered was methylated with CH_2N_2 to yield methyl 7,8,16,18-tetraacetoxyserrulatan-19-oate (**3**, 157 mg) mp 127–128°, bp 225–235° (bath)/0.15 mm; $[\alpha]_D$ −17.4° (*c* 1.08; $CHCl_3$). (Found: C, 63.46; H, 7.59. $C_{29}H_{40}O_{10}$ requires C, 63.47; H, 7.35%.) IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1789, 1785, 1750, 1740, 1735; ^{1}H NMR ($CDCl_3$, 90 MHz): δ0.86 (3H, *d*, J = 6.5 Hz, Me-17), 1.17 (3H, *d*, J = 7 Hz, Me-20), 2.03, 2.06 (*s*) and 2.31, 233 (12H, *s*, OAc), 3.0 (2H, *m*, $W_{1/2}$ = 13 Hz, H-4 and H-1), 3.88 (3H, *s*, OMe), 3.73–3.94 (2H, *m*, 16-H_2), 4.08 (2H, AB part of ABX, 18-H_2), 7.29 (1H, *s*, H-5). MS m/z (rel. int.): 548 $[M]^+$ (1) 516 (3), 505 (4), 473 (9), 464 (2), 446 (23), 413 (19), 404 (40), 372 (25), 277 (80), 245 (35), 235 (100), 202 (81). (b) A sample of **2** (152 mg) in Me_2CO (5 ml) was treated with excess dimethyl sulphate and K_2CO_3 (60 mg) and the soln left stirring for 36 hr. The product recovered with CH_2Cl_2 was purified by adsorption on a column of alumina (act III, neutral). Elution with EtOAc–CH_2Cl_2 (4:1) gave methyl 16,18-dihydroxy-7,8-dimethoxyserrulatan-19-oate (**4**) (54 mg) as a colourless oil, bp 190–195° (bath)/0.2 mm; $[\alpha]_D$ −24.4° (*c* 0.8; $CHCl_3$). (Found: C, 67.60; H, 9.03. $C_{23}H_{36}O_6$ requires C, 67.60; H, 8.89%.) IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3620, 1735; ^{1}H NMR ($CDCl_3$, 90 MHz): δ0.81 (3H, *d*, J = 7 Hz, Me-17), 1.19 (3H, *d*, J = 7 Hz, Me-20), 3.00 (2H, *m*, $W_{1/2}$ = 12 Hz, H-1 and H-4), 3.36 and 3.62 (4H, centres of AB parts of ABX systems, 16-H_2 and 18-H_2 respectively), 3.87 and 3.88 (6H, *s*, OMe), 7.46 (1H, *s*, H-5). MS m/z (rel. int.): 408 $[M]^+$ (12), 376 (13), 264 (17), 263 (100), 231 (153).

Correlation of **2** *with* 7,8-*dimethoxyserrulatan*-19-*ol.* (**5**). A sample of **4** (112 mg) in C_5H_5N (1 ml) was treated with excess toluene-*p*-sulphonyl chloride for 33 hr. The ditosylate (176 mg) recovered was dissolved in Et_2O (5 ml) and was added dropwise

to a stirred soln of $LiAlH_4$ (95 mg) in Et_2O and the mixture was left for 24 hr under N_2. The product was adsorbed on a column of alumina (act III, neutral) and elution with CH_2Cl_2–EtOAc (3:2) gave a fraction (25 mg) which was further purified by prep. TLC (EOAc) to give the benzyl alcohol (**5**, 10 mg) $[\alpha]_D$ −35.1° (*c* 0.9; $CHCl_3$) (lit. [5] $[\alpha]_D$ −39°) identical with an authentic sample [5].

Dehydrogenation of **3** *with DDQ.* A sample of **3** (120 mg) in C_6H_6 and DDQ (400 mg) was heated under reflux for 18 hr under N_2. The reaction mixture was cooled, filtered and the solvent evaporated. The residue was adsorbed on a column of Al_2O_3 (act III, neutral) and elution with CH_2Cl_2 to EtOAc gave methyl (2′*S*,6′*S*)-3,4-diacetoxy-8-(1′,7′-diacetoxy-6′-methylheptan-2′-yl)-5-methylnaphthalene-2-carboxylate (**8**, 52 mg) as a colourless oil, $[\alpha]_D$ +2.9° (*c* 2.1; $CHCl_3$). (Found: $[M]^+$ 544.232; $C_{29}H_{36}O_{10}$ requires $[M]^+$ 544.231). IR ν_{max} cm^{-1}: 1790, 1785, 1755, 1750, 1740; UV λ_{max}^{MeOH} nm: (log ε): 252 (4.36), 293 (3.94), 305 (3.87), 346 (3.67). ^1H NMR ($CDCl_3$, 90 MHz): δ0.81 (3H, *d*, *J* = 7 Hz, Me-17), 1.88, 1.90, 2.28, 2.31 (12H, *s*, OAc), 2.71 (3H, *s*, Me-20); 3.66–3.94 (2H, *m*, H-18a and H-11), 3.89 (3H, *s*, OMe), 3.77 (2H, AB part of ABX, 16-H_2), 4.21 (1H, *d br*, H-18b), 7.24 (2H, *s*, H-2 and H-3), 8.79 (1H, *s*, H-5). MS *m/z* (rel. int.): 544 $[M]^+$ (1), 516 (20), 502 (1), 474 (31), 460 (30), 445 (52), 413 (50), 404 (98), 372 (50), 277 (72), 235 (100), 203 (80).

Oxidation of the methyl ester derivative of **2** *with Fremy's salt.* A sample of **2** (120 mg) was methylated with CH_2N_2 and the methyl ester recovered was dissolved in Me_2CO (5 ml) and treated with Fremy's salt (100 mg) in phosphate buffer (0.05 M KH_2PO_4; 5 ml) with stirring under N_2 for 4 days. The product (90 mg) recovered with CH_2Cl_2 was a red oil with spectral characteristics indicative of a quinone ether; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3560 1735 1670; UV λ_{max}^{EtOH} nm (log ε): 234 (4.44), 289 (4.34), 450 (3.68), 255 (4.43). ^1H NMR ($CDCl_3$, 60 MHz): δ0.87 (3H, *d*, *J* = 6 Hz, Me-17), 1.11 (3H, *d*, *J* = 6.5 Hz, Me-20) 2.75–3.05 (2H, *m*, H-1 and H-4), 3.35 (2H, AB part of ABX, 16-H_2), 3.60–4.04 (1H, *m*, H-18a); 3.70 (3H, *s*, OMe), 4.47 (2H, *dd*, *J* = 3 and 10 Hz, H-18b). MS *m/z* (rel. int.): 378 $[M+2]^+$, (5), 360 (12), 328 (12), 279 (33), 249 (77), 217 (37), 167 (23), 149 (81), 57 (100). The *quinone ether* (80 mg), Ac_2O (1 ml), Zn powder (90 mg) and NaOAc (10 mg) were stirred at room temp. for 2 days. The product recovered was filtered through silicic acid to give a yellow oil which crystallized from $CHCl_3$–pentane as colourless needles of methyl (15*S*)-7,8,16-triacetoxy-5,18-epoxyserrulatan-19-oate (**10**) mp 150–152°; $[\alpha]_D$ −12.9° (*c* 0.1; $CHCl_3$). (Found: C, 63.92; H, 7.35. $C_{27}H_{36}O_9$ requires C, 64.26; H, 7.20%.) IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1795, 1785, 1750, 1740; ^1H NMR ($CDCl_3$, 80 MHz): δ0.93 (3H, *d*, *J* = 6.5 Hz, Me-17), 1.20 (3H, *d*, *J* = 7 Hz, Me-20) 2.06, 2.22, 2.27 (9H, *s*, OAc), 2.80–3.15 (2H, *m*, H-1 and H-4), 3.67–3.98 (3H, *m*, 16-H_2 and H-18a), 4.37 (1H, *dd*, *J* = 3.5 and 11 Hz, H-18b), 3.84 (3H, *s*, OMe); ^{13}C NMR: Table 1. MS *m/z* (rel. int.): 504 $[M]^+$, (1), 462 (5), 420 (28), 389 (25), 388 (100), 378 (2), 360 (2), 346 (4).

Major metabolites from E. woolsiana. A sample of the flowering plant (159 g) collected in October 1980 36 km from Corrigin to Bendering in Western Australia yielded $NaHCO_3$-soluble (17.4 g), 5% aq. NaOH-soluble (1.40 g) and neutral (1.86 g) fractions. A portion (10 g) of the bicarbonate extract after chromatography yielded the tetrahydroxy acid **2** (1.45 g), the monoacetate (1.89 g) and the diacetate (1.20 g) derivatives identical with those isolated from *E. drummondii* var. *brevis*.

Isolation of the major metabolites from E. glabra. A sample of the flowering plant (450 g) collected in September 1982, 98.6 km north of Mt. Magnet in Western Australia yielded $NaHCO_3$-soluble (21.4 g), 5% aq. NaOH-soluble (8.8 g) and neutral (3.49 g) fractions. A portion (1.99 g) of the NaOH solubles was filtered through neutral charcoal in EtOAc and the fraction obtained (1.06 g) was fractionated by RSF. Elution with CH_2Cl_2–EtOAc (1:4) gave 8,20-dihydroxyserrulat-14-en-19-oic acid (**11**) (322 mg) which crystallized from EtOAc–pentane as pale orange crystals, mp 123–125°, $[\alpha]_D$ −38.1 (*c* 0.4; $CHCl_3$). (Found: C, 72.40; H, 8.62. $C_{20}H_{28}O_4$ requires: C, 72.25; H, 8.49%.) IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3600, 1685; ^1H NMR (80 MHz, $CDCl_3$): δ1.02 (3H, *d*, *J* = 7 Hz, Me-18), 1.54 and 1.64 (6H, *s*, Me-16 and Me-17), 2.56 (1H, *m*, $W_{1/2}$ = 10 Hz, H-4), 3.38 (1H, *m*, $W_{1/2}$ = 14 Hz, H-1), 3.88 (2H, AB part of ABX, 20-H_2), 4.98 (1H, *t br*, *J* = 7 Hz, H-14), 7.44 (1H, *d*, *J* = 2 Hz, H-7), 7.58 (1H, *d*, *J* = 2 Hz, H-5). MS *m/z* (rel. int.): 332 $[M]^+$ (31), 314 (15), 248 (11), 222 (25), 203 (36), 69 (100). Similar fractionation of the $NaHCO_3$-soluble fraction yielded 8,20-diacetoxyserrulat-14-en-19-oic acid (**12**, 3.16 g) as an oil, $[\alpha]_D$ −30.8° ($CHCl_3$; *c* 1.7). (Found: $[M]^+$ 416.218. $C_{24}H_{33}O_6$ requires: $[M]^+$ 416.2199.) IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3500, 1750, 1700; ^1H NMR (90 MHz, $CDCl_3$): δ1.00 (3H, *d*, *J* = 7 Hz, Me-18), 1.55 and 1.65 (6H, *s*, Me-16 and Me-17), 2.05, 2.38 (6H, *s*, OAc), 2.73 (1H, *m*, $W_{1/2}$ = 12 Hz, H-4), 3.17–3.48 (1H, *m*, H-1), 3.84 (1H, *t*, *br*, *J* = 10 Hz, H-20a), 4.35 (1H, *dd*, *J* = 4 and 10 Hz, H-20b), 4.97 (1H, *t br*, *J* = 7 Hz, H-14), 7.65 (1H, *d br*, *J* = 1.5 Hz, H-5), 7.86 (1H, *d br*, *J* = 1.5 Hz, H-7). ^{13}C NMR: Table 1. MS *m/z* (rel. int.): 416 $[M]^+$, (29), 356 (46), 328 (25), 314 (42), 273 (29), 245 (32), 201 (46), 108 (100), 69 (67). Treatment of **12** with CH_2N_2 yielded methyl 8,20-diacetoxyserrulat-14-en-19-oate as an oil, bp 150–165° (bath)/0.2 mm, $[\alpha]_D$ −24.7° (*c* 0.7; $CHCl_3$). (Found: C, 69.48; H, 7.83. $C_{25}H_{34}O_6$ requires: C, 69.74; H, 7.96%.) IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1775, 1740, 1725. MS *m/z* (rel. int.): 430 $[M]^+$ (6), 370, (10), 328 (15), 261 (10), 218 (25), 69 (100).

Correlation of **11** *with* 8-*methoxyserrulatane* (**16**). A sample of **11** (223 mg) and K_2CO_3 in Me_2CO was treated with excess MeI to give methyl 20-hydroxy-8-methoxyserrulat-14-en-19-oate (**13**, 185 mg) as an oil, bp 155–160° (bath)/0.6 mm, $[\alpha]_D$ −60.5° (*c* 0.4; $CHCl_3$). (Found: C, 73.12; H, 8.90. $C_{22}H_{32}O_4$ requires: C, 73.30; H, 8.95%.) ^1H NMR ($CDCl_3$, 80 MHz): δ0.98 (3H, *d*, *J* = 7 Hz, Me-18), 1.54 and 1.62 (6H, Me-16 and Me-17), 2.65 (2H, *m*, $W_{1/2}$ = 11 Hz, H-4), 3.35 (1H, *m*, $W_{1/2}$ = 7 Hz, H-1), 3.53 (1H, *t*, *J* = 10 Hz, H-20a), 3.79 (1H, *dd*, *J* = 4 and 10 Hz, H-20b), 3.88, 3.90 (6H, *s*, OMe), 4.96 (1H, *t br*, *J* = 7 Hz, H-14), 7.35 and 7.53 (2H, *s*, H-5 and H-7). MS *m/z* (rel. int.): 360 $[M]^+$, (100), 342 (50), 231 (70). Compound **13** (150 mg) in C_5H_5N was treated with toluene-*p*-sulphonyl chloride (160 mg) for 21 hr to yield the tosylate **14** (175 mg). MS *m/z* (rel. int.): 514 $[M]^+$ (2), 342 (13), 231 (100). The tosylate **14** (420 mg) in Et_2O (50 ml) and $LiAlH_4$ (2 g) were stirred under reflux for 4 hr. Recovery of the product with Et_2O gave 19-hydroxy-8-methoxyserrulat-14-ene (**15**, 263 mg), bp 160° (bath)/0.1 mm, $[\alpha]_D$ −46.5° (*c*, 0.8; $CHCl_3$). (Found: C, 80.03; H, 10.35. $C_{21}H_{32}O_2$ requires: C, 79.70; H, 10.19%.) Compound **15** (121 mg) in EtOH (50 ml) was stirred under an H_2 atmosphere over 10% Pd–C for 18 hr. Filtration and evaporation of the solvent gave a compound (109 mg), $[\alpha]_D$ −41° (*c* 1.6; $CHCl_3$), identical with an authentic sample of 8-methoxyserrulatane (**16**) [6].

Isolation of metabolites from E. denticulata *and* E. decipiens. A sample of flowering *E. denticulata* (440 g) obtained in September 1979 from Xanthorrhea Nursery, Lesmurdie in Western Australia, was extracted with Et_2O. The ethereal soln was washed with 8% of $NaHCO_3$ to give a compound (13.5 g) identical with **11**. The major acidic component (1.25 g) of an extract (10.65 g) of a sample (500 g) of *E. decipiens* in flower, collected in October 1975, 62 km from Morawa to Pindar in Western Australia, was found to be identical with **11**.

Isolation of metabolites from E. hughesii. A sample of the flowering plant (44 g), collected in September 1982 57 km east of Meekatharra in Western Australia yielded $NaHCO_3$-soluble (100 mg), 5% aq. NaOH-soluble (3.1 g) and neutral (450 mg) fractions. RSF chromatography of the NaOH soluble fraction

and elution with EtOAc–CH_2Cl_2 (3:2) to EtOAc gave fractions (928 mg) containing the tetraol. A portion (115 mg) was purified by prep. TLC (Me_2CO (*iso*-Pr)$_2$O–AcOH, 19:80:1) and recrystallized from (*iso*-Pr)$_2$O–petrol as brown prisms, mp 84–86°, $[\alpha]_D$ 4.5° (*c* 1.2; $CHCl_3$); −9.9° (*c* 1.2, EtOH) identical with an authentic sample of **17** mp 83–85 mmp 83–85°, $[\alpha]_D$ +2.9 (*c* 0.3; $CHCl_3$); −9.0° (*c* 0.3; EtOH). Filtration of the $NaHCO_3$-soluble fraction through charcoal gave a diacetoxy acid (40 mg) identical with **12** previously isolated from *E. glabra*.

Isolation of metabolites from E. gibsonii. A sample of the flowering plant (925 g) collected in September 1982 11 km north of Meekatharra in Western Australia yielded 5% aq. NaOH (13.6 g) and neutral (700 mg) fractions. RSF of a portion (3 g) of the NaOH-soluble fraction and elution with EtOAc gave 2,8,20-trihydroxyserrulat-14-ene (**18**, 807 mg) which crystallized from (*iso*-Pr)$_2$O–pentane as pale orange prisms, mp 110–112°, $[\alpha]_D$ −21.5° (*c* 1.2; $CHCl_3$). (Found: $[M]^+$ 318.219. $C_{20}H_{30}O_3$ requires $[M]^+$ 318.2195). IR $\nu_{max}^{CS_2}$ cm^{-1}: 3600 ^{1}H NMR (80 MHz, $CDCl_3$): δ1.06 (3H, *d*, *J* = 6.5 Hz, Me-18), 1.59 and 1.70 (6H, *s*, Me-16 and Me-17), 2.24 (3H, *s*, Me-19), 2.50 (1H, *m*, $W_{1/2}$ = 20 Hz, H-4), 3.10 (1H, *m*, $W_{1/2}$ = 12 Hz, 1-H), 3.75–4.15 (2H, *m*, 20-H$_2$), 5.08 (1H, *t*, *br*, *J* = 7 Hz, 14-H), 6.54 and 6.66 (2H, *s br*, 5-H and 7-H). MS *m/z* (rel. int.): 318 $[M]^+$ (14), 300 (31), 190 (36), 175 (29), 159 (100). Later fractions afforded an oil which was acetylated (C_5H_5N–Ac_2O) and the product purified by chromatography on Al_2O_3. Elution with CH_2Cl_2 gave the tetraacetate (283 mg) identical with that previously prepared from the tetraol (**17**) [5].

Derivatives of **18**. (a) A sample of **18** (250 mg) in Me_2CO (8 ml) was treated with K_2CO_3 (110 mg) and excess MeI for 22 hr. Recovery of the product gave 2,20-dihydroxy-8-methoxyserrulat-14-ene (**19**, 200 mg) as an oil, bp 175–180° (bath)/0.2 mm, $[\alpha]_D$ −58° (*c*, 4.9, $CHCl_3$). (Found: C, 75.55; H, 9.50. $C_{21}H_{32}O_3$ requires: C, 75.86; H, 9.70%.) ^{1}H NMR: essentially the same as that of except for the prence of an extra signal at δ3.78 (OMe). MS *m/z* (rel. int.): 332 $[M]^+$ (18), 314 (9), 284 (18), 203 (21), 174 (100). (b) A soln of **18** (1.5 g) in Et_2O (200 ml) was treated with paraldehyde (4 ml) and conc. HCl (20 drops) and the mixture was stirred at room temp. for 31 hr. The product recovered was purified by RSF chromatography and elution with CH_2Cl_2 to EtOAc gave the ethylidene (**20**, 214 mg) as an oil, $[\alpha]_D$ −36.8° (*c* 1.8; $CHCl_3$). (Found: $[M]^+$ 334.235. $C_{22}H_{32}O_3$ requires: $[M]^+$ 344.235.) ^{1}H NMR (90 MHz, $CDCl_3$): δ1.02 (3H, *d*, *J* = 7 Hz, Me-18), 1.39 (3H, *d*, *J* = 5 Hz, ethylidene methyl protons), 1.52 and 1.62 (6H, *s*, Me-16 and Me-17), 2.21 (3H, *s*, Me-19), 2.74–3.23 (2H, *m*, H-1 and H-4), 3.40–3.78 (1H, *m*, H-2) 3.59 (1H, *dd*, *J* = 12 Hz and 12 Hz, H-20a) 4.42 (1H, *q*, *J* = 5 Hz, acetal methine), 4.70–5.04 (1H, *m*, H-14), 5.41 (1H, *dd*, *J* = 4 Hz and 12 Hz, H-20b), 6.35 and 6.65 (2H, *s*, H-5 and H-7). MS *m/z* (rel. int.): 344 $[M]^+$ (58), 300 (58), 282 (26), 269 (21), 189 (63), 159 (100).

Isolation of metabolites from E. virens. A sample (237 g) of the flowering plant, collected in October 1980 at Weira Road Junction, Western Australia, after extraction and fractionation yielded $NaHCO_3$-soluble (5.7 g), NaOH-soluble (8.2 g) and neutral (8.25 g) fractions. The neutral fraction contained mainly (1*R*,4*R*)-calamenene and (1*R*,4*R*)-7-hydroxycalamenene [10]. The NaOH-soluble fraction was taken up in Et_2O, filtered through charcoal to remove flavonoid components and then subjected to RSF chromatography. Elution with CH_2Cl_2–EtOH (2:3) gave the dihydroxy acid **11** (1.5 g), mp 122–124°, undepressed on admixture with a sample isolated from *E. glabra*. RSF chromatography of the $NaHCO_3$-soluble fraction and elution with CH_2Cl_2–EtOAc (3:7) gave fractions (830 g) of 8,20-dihydroxy-14-oxo-serrulatan-19-oic acid (**21**) as an oil. (Found: 330.179. $C_{20}H_{28}O_5$ requires $[M-18]^+$ 330.183.) Methylation with CH_2N_2 afforded the methyl ester as an oil, $[\alpha]_D$ −36.8° (*c* 4.3; $CHCl_3$). (Found: 332.197, $C_{21}H_{30}O_5$ requires $[M-30]^+$ 332.1987.) IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3640, 1731; ^{1}H NMR ($CDCl_3$, 90 MHz): δ0.95 (6H, *d*, *J* = 6 Hz, Me-16 and Me-17), 1.02 (3H, *d*, *J* = 7 Hz, Me-18), 3.34 (1H, *m*, $W_{1/2}$ = 15 Hz, H-1), 3.60–3.94 (2H, *m*, 20-H$_2$), 3.84 (2H, *s*, OMe) 7.35 and 7.42 (2H, *d*, *J* = 2 Hz, H-5 and H-7). ^{13}C NMR: Table 1. MS *m/z* (rel. int.): 362 $[M]^+$ (1), 332 (23), 330 (11), 300 (100), 299 (28), 185 (35). Acetylation of **22** with Ac_2O–pyridine gave methyl 8,20-diacetoxy-14-oxo-serrulatan-19-oate (**23**), oil, $[\alpha]_D$ −26.5° (*c* 0.3; $CHCl_3$). (Found: 386.203. $C_{25}H_{36}O_7$ requires $[M-AcOH]^+$ 386.209.) ^{1}H NMR (90 MHz, $CDCl_3$): δ0.95 (3H) and 1.07 (6H, *d*, *J* = 6 Hz, Me-16, 17, 18), 2.05 and 2.38 (6H, *s*, OAc), 3.30 (1H, *m*, H-1), 3.82 (1H, *dd*, *J* = 10.5 Hz, H-20a), 3.88 (3H, *s*, OMe), 4.31 (1H, *dd*, *J* = 10.5 Hz, *J* = 4 Hz, H-20b), 7.58 and 7.78 (2H, *d*, *J* = 2 Hz, H-5 and H-7). ^{13}C NMR: Table 1. MS *m/z* (rel. int.): 446 $[M]^+$ (1), 415 (2), 386 (4), 326 (21), 217 (51), 185 (43), 127 (100).

Conversion of **12** *to* **23**. A sample of **12** was treated with CH_2N_2 and the methyl ester (615 mg) in dry Et_2O (5 ml) was stirred with $BH_3 \cdot Me_2S$ (215 μl, 2.15 mmol) at 0° for 1 hr under N_2. EtOH (0.2 ml) was slowly added followed by 30% aq. NaOH soln (1 ml) and 30% H_2O_2 (1 ml) and the mixture was stirred for 1 hr, poured into 10% HCl and extracted with Et_2O. The product recovered (680 mg) was stirred with pyridinium dichromate (5.6 g) in dry CH_2Cl_2 for 24 hr at room temp. The soln was filtered through silicic acid to give the keto-ester (**23**), oil, $[\alpha]_D$ −25.8° (*c* 0.3; $CHCl_3$) identical by ^{1}H NMR and ^{13}C NMR, MS, IR and $[\alpha]_D$ with a sample of **23** prepared as described above.

Isolation of metabolite from E. biserrata. A sample (204 g) of the flowering plant collected in November 1980 by Mr. Chinnock, South Australian Herbarium, yielded $NaHCO_3$-soluble (4.26 g), NaOH-soluble (5.57 g) and neutral (3.0 g) fractions. A portion of the NaOH-soluble fraction was chromatographed by RSF and a fraction containing mainly diterpene was treated with CH_2N_2. A sample of the crude monomethyl ether (100 mg) was purified by prep. TLC to give methyl (15*S*)-16-hydroxyserrulatan-19-oate (72 mg) as an oil $[\alpha]_D$ −89° (*c* 1.3; $CHCl_3$) identical with an authentic sample of **24** [5].

Isolation of **25** *from* E. recemosa. A sample of the flowering plant (184 g) collected in October 1980 9 km north of Lake Cronin in Western Australia was extracted with MeOH to give a viscous green oil which was partitioned into Et_2O-soluble (2.4 g) and Et_2O-insoluble (2.69 g) fractions. The residue was recrystallized from EtOH to give colourless needles of phillyrin (**25**), mp 148–150°, $[\alpha]_D$ +47.5° (*c* 0.2; MeOH) (lit. [9] mp 146–148° $[\alpha]_D$ +46.9°). A soln of (190 mg) in H_2O (150 ml) was treated with emulsin and thymol (7 mg) for 3 days at 38°. The material extracted with $CHCl_3$ crystallized from MeOH as needles of phillygenin (100 mg), mp 134–135°, $[\alpha]_D$ +117.3° (*c* 0.2; MeOH) (lit. [9] mp 133–134°, $[\alpha]_D$ +120°). The ^{13}C NMR spectrum of phylligenin was identical with that reported [11].

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