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# TERPENOID AND FLAVONE CONSTITUENTS OF *POLEMONIUM VISCOSUM*

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**Key Word Index**—*Polemonium viscosum*; Polemoniaceae; labdane diterpenes; flavone; monoterpene glycosides; $^{13}C$ NMR investigation; X-ray structure.

**Abstract**—The chemical investigation of *Polemonium viscosum* yielded several new diterpenes with labdane and pimarane skeletons, a new flavone and two new monoterpene glycosides. The absolute configuration of akhardiol is established by X-ray structure determination of the O-bromobenzoate derivative.

## INTRODUCTION

*Polemonium viscosum* or sky pilot lives on open rocky ridges in high mountains. The plant exudes a very pungent, skunk-like scent from the sticky, glandular hairs that cover its leaves and stems. We have found *P. viscosum* to be a very rich source for a variety of natural products. There are quite a few reports in the literature on compounds from other *Polemonium* species. This genus of plant produces a great variety of triterpene saponins [1, 2]. No other small terpenes have been reported from *Polemonium*.

## RESULTS AND DISCUSSION

Fresh, whole plants of *P. viscosum* were extracted with ethyl acetate. The crude extract was initially fractionated by silica gel column chromatography. The least polar diterpene to elute was compound **1**. High resolution mass spectrometry established the molecular formula of **1** as $C_{22}H_{36}O_3$. The $^1H$ NMR methyl singlet at $\delta$2.05 and the IR absorbance at 1730 $cm^{-1}$ indicated an acetylated diterpene derivative. The molecular formula showed four other sites of unsaturation, one of these sites being a monosubstituted double bond ($^{13}C$ NMR resonances at $\delta$110.3 *t* and 148.0 *d*). Of the three additional sites, one was a cyclic ether ($^{13}C$ NMR resonances at $\delta$73.2 *s* and 74.8 *s*). This data indicated a labdane skeleton. Through comparison of the chemical shifts of the proton methyl resonances and the olefinic protons, compound **1** was determined to be a manoyl oxide derivative [3] with one of the methyl groups oxidized and acetylated. The position of oxidation was established by consideration of the $^1H$ NMR and $^{13}C$ NMR shifts of the methyl resonances and comparison of these to manoyl oxide (**3**) (Tables 1 and 2). It is clearly seen that oxidation occurs at one of the methyls at C-4. Comparison of the $^{13}C$ NMR shifts to that of 19-hydroxy-2- ketomanoyl oxide indicated that the $CH_2$-OAc group was at C-19 [4]. Alkaline hydrolysis of **1** yielded the primary alcohol **2** which was identical to the next diterpene that eluted from the column.

The most polar fraction that eluted from the silica gel

Table 1. $^1H$ NMR spectral data of the methyl resonances of diterpenes **1,2** and **3**

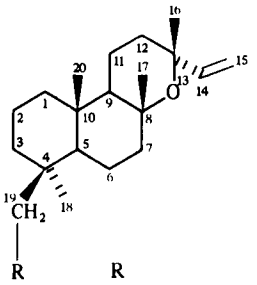
| C | 1 | 2 | 3* |
|---|---|---|---|
| 16 | 1.26 | 1.26 | 1.27 |
| 17 | 1.26 | 1.26 | 1.27 |
| 18 | 0.80 | 0.80 | 0.78 |
| 19 | † | † | 0.78 |
| 20 | 0.96 | 0.96 | 0.85 |

*Ref. [3].
†Oxidized position.

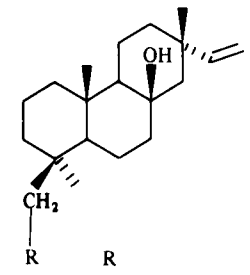
Table 2. $^{13}C$ NMR spectral data of diterpenes **1–4, 6** and **7**

| C | 1 | 2 | 3* | 4 | 6 | 7* |
|---|---|---|---|---|---|---|
| 1 | 38.9 *t* | 39.1 *t* | 38.9 | 36.3 *t* | 39.7 *t* | 39.4 |
| 2 | 18.1 *t* | 18.1 *t* | 18.4 | 18.0 *t* | 18.4 *t* | 18.2 |
| 3 | 36.4 *t* | 38.5 *t* | 41.9 | 35.5 *t* | 42.0 *t* | 41.7 |
| 4 | 36.4 *s* | 35.7 *s* | 32.5 | 37.0 *s* | 33.1 *s* | 33.0 |
| 5 | 55.7 *d* | 55.7 *d* | 55.5 | 56.9 *d* | 56.1 *d* | 55.8 |
| 6 | 20.1 *t* | 20.1 *t* | 19.8 | 17.8 *t* | 19.1 *t* | 18.7 |
| 7 | 43.5 *t* | 43.6 *t* | 42.6 | 43.8 *t* | 44.8 *t* | 44.7 |
| 8 | 74.8 *s* | 74.9 *s* | 74.9 | 72.3 *s* | 74.1 *s* | 74.5 |
| 9 | 57.0 *d* | 57.0 *d* | 56.2 | 57.0 *d* | 61.9 *d* | 61.5 |
| 10 | 36.9 *s* | 36.9 *s* | 36.7 | 38.5 *s* | 39.3 *s* | 38.9 |
| 11 | 15.4 *t* | 15.4 *t* | 15.2 | 17.0 *t* | 20.5 *t* | 20.1 |
| 12 | 35.5 *t* | 35.6 *t* | 35.5 | 37.9 *t* | 44.1 *t* | 43.8 |
| 13 | 73.2 *s* | 73.2 *s* | 73.0 | 39.4 *s* | 75.0 *s* | 73.1 |
| 14 | 148.0 *d* | 147.9 *d* | 147.8 | 151.4 *d* | 145.2 *d* | 146.6 |
| 15 | 110.3 *t* | 110.2 *t* | 110.0 | 108.4 *t* | 111.8 *t* | 110.5 |
| 16 | 28.6 *q* | 28.5 *q* | 28.4 | 26.9 *q* | 25.6 *q* | 26.0 |
| 17 | 25.3 *q* | 25.3 *q* | 25.4 | 51.3 *t* | 24.4 *q* | 23.9 |
| 18 | 27.3 *q* | 26.9 *q* | 32.5 | 24.1 *q* | 33.3 *q* | 33.0 |
| 19 | 67.0 *t* | 65.2 *t* | 21.3 | 64.9 *t* | 21.4 *q* | 21.2 |
| 20 | 15.7 *q* | 15.8 *q* | 16.6 | 16.1 *q* | 15.2 *q* | 15.1 |
| AC | 171.3 *s* | | | | | |
| | 20.8 *q* | | | | | |

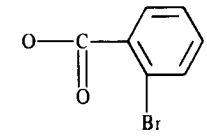
*Ref. [4].



| | R |
|---|---|
| **1** | OAc |
| **2** | OH |
| **3** | H |



| | R |
|---|---|
| **4** | OH |



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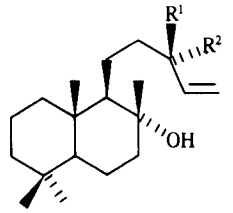
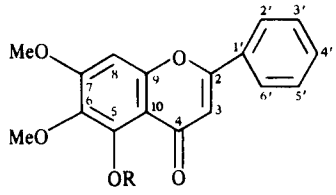
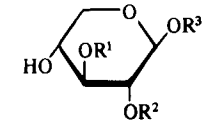
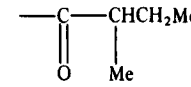
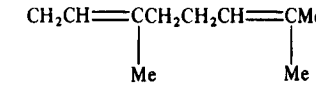
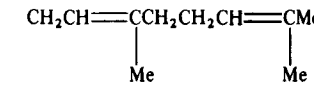
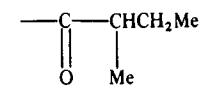
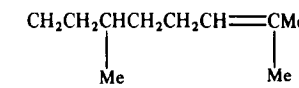
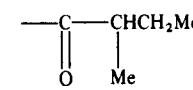
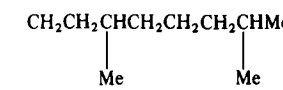


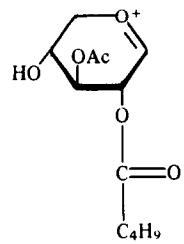
| | $R^1$ | $R^2$ |
|---|---|---|
| **6** | OH | Me |
| **7** | Me | OH |



| | R |
|---|---|
| **8** | H |
| **9** | Ac |



| | $R^1$ | $R^2$ | $R^3$ |
|---|---|---|---|
| **10** | Ac |  |  |
| **11** | H | H |  |
| **12** | Ac |  |  |
| **13** | Ac |  |  |



**14**

column was a mixture of components that could be separated by HPLC on silica gel. The least polar diterpene in this group, compound **4**, had a molecular formula of $C_{20}H_{34}O_2$ which was established by high resolution mass spectrometry. Compound **4** contained a monosubstituted double bond (Table 2) and three carbocylic rings. This data indicated a pimarane skeleton. In order to establish the stereochemistry of **4** an X-ray analysis was undertaken. Alcohol **4**, its acetate and *p*-bromobenzoate derivatives all gave very small fractured crystals. The *o*-bromobenzoate derivative, compound **5**, however, gave satisfactory crystals for the analysis. A thermal ellipsoid drawing of the molecular structure of **5** is presented in Fig. 1. The indicated absolute configuration was determined by analysis of the crystallographic data. Compound **4** was found to be identical to akhdardiol, which has been recently isolated from *Amaracus akhdarensis* [5].

The most polar diterpene to be eluted from the HPLC was a diol, compound **6**, $C_{20}H_{36}O_2$. The spectral data on this compound was very close to sclareol (**7**) [6] (Table 2). The major difference in the $^{13}C$ NMR spectra were several of the resonances around C-13. This indicated that **6** was an epimer of sclareol at C-13. The physical properties of **6** (125–127°, $[\alpha]_D + 6.6°$) and those reported

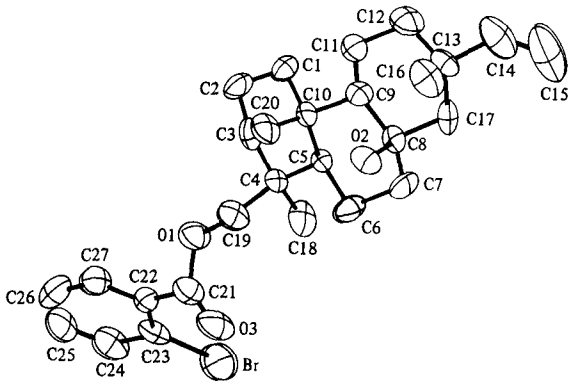



Fig. 1.

for 13-episclareol (mp 129–130°, $[\alpha]_D + 11.0°$) [7] are very close. There have been no published reports on the $^1H$ NMR or $^{13}C$ NMR of 13-episclareol.

The only flavonoid to elute from the HPLC had a molecular formula of $C_{17}H_{14}O_5$ (high resolution mass spectrometry). The UV spectrum of **8** had maxima at 314, 272 and 248 nm. This spectrum, coupled with the singlet at $\delta$6.60 in the $^1H$ NMR spectrum, indicated a flavone [8]. The $^1H$ NMR multiplets at $\delta$7.53 (3H) and 7.92 (2H) indicated that the B-ring was unsubstituted [9]. An additional aromatic proton singlet at $\delta$6.70 indicated that the A-ring had three other substituents. Two of these were methoxyls which appeared at $\delta$3.95 and 4.01 in the $^1H$ NMR spectrum. The third substituent was inferred to be a phenol by the strong IR absorption at 3500 $cm^{-1}$. Acetylation of **8** gave a monoacetate, **9**. The only change in the $^1H$ NMR spectrum, besides the addition of the acetate singlet at $\delta$2.47, was a small downfield shift (0.22) of the C-8 proton. This shift is expected for an aromatic proton *ortho* or *para* to a phenolic group [10]. Calculation of the $^{13}C$ NMR shifts around ring A for the different possible substitution patterns indicated that the 5,6,7-trioxygenation pattern was the most likely (Table 3). Comparison of the $^{13}C$ NMR shifts in the 6,7-dimethoxy-5-hydroxy-flavone system of salvigenin also demonstrated this oxygenation pattern (Table 3). The placement of the hydroxy group in **8** was done by recording the UV spectrum in MeOH, MeOH–$AlCl_3$ and MeOH–$AlCl_3$–HCl [11]. The $\lambda_{max}$ of 246, 270 and 314 mm in **8** shifted to 254, 284 and 340 when $AlCl_3$ was added. These shifts remained when HCl was added. These bathochromic shifts are characteristic of a free 5-hydroxy flavone. The structure of **8** was then deduced to be 6,7-dimethoxy-5-hydroxyflavone. This is a very unusual flavone which contains a highly oxygenated A-ring and no oxygenation in the B-ring.

Two of the more polar compounds to be purified by HPLC had very different spectra than the other components. The highest mass peak seen in the EI, CI and FAB mass spectrum of **10**, the more polar component, was *m/z* 259. The molecular formula of $C_{22}H_{36}O_7$ was established by elemental analysis. The large number of $^1H$ NMR signals from $\delta$3–5 and the $^{13}C$ NMR resonance at $\delta$99.5 indicated a glycoside. The $^1H$ NMR broadened methyl singlets at $\delta$1.63, 1.68 and 1.71 and broadened triplets at 5.10 and 5.25 indicated that the monoterpene geraniol was attached to the sugar [15]. Acid hydrolysis of **10** gave components in the organic and aqueous phases. Analysis

Table 3. $^{13}C$ NMR spectral data of **8** and selected flavones.

| C | 8 | Calculated* | | |
|---|---|---|---|---|
| 2 | 163.9 *s* | | 163.1† | |
| 3 | 105.5 *d* | | 102.9 | |
| 4 | 182.7 *s* | | 181.5 | |
| 5 | 158.9 *s* | 148.0 | 158.1 | |
| 6 | 132.7 *s* | 125.0 | 132.0 | |
| 7 | 153.3 *s* | 147.0 | 152.0 | |
| 8 | 90.6 *d* | 94.7 | 91.0 | |
| 9 | 153.0 *s* | 154.6 | 151.7 | |
| 10 | 106.2 *s* | 103.0 | 104.9 | |
| 1′ | 131.2 *s* | 130.6 | | 130.8‡ |
| 2′ | 126.2 *d* | 129.6 | | 126.0 |
| 3′ | 129.0 *d* | 128.6 | | 128.7 |
| 4′ | 131.8 *d* | 133.0 | | 131.4 |
| 5′ | 129.0 *d* | 128.6 | | 128.7 |
| 6′ | 126.2 *d* | 129.6 | | 126.0 |
| OMe | 56.3 *q* | | | |
| OMe | 60.8 *q* | | | |

*Calculated from the tables in Ref. [12].
†Salvigenin (4′,6,7-trimethoxy-5-hydroxyflavone) (Rings A and C) Ref. [13].
‡Flavone (Ring B). Ref. [14].

of the organic extract by GC-MS and comparison with known compounds demonstrated that geraniol was indeed present ($M^+$, retention time). Paper chromatographic analysis of the aqueous phase of the acid hydrolysis in three different solvent systems demonstrated that the sugar moiety was xylose [16]. The rotation indicated the D-isomer. In addition to the geraniol moiety the xylose was esterified with an acetate (IR 1740 $cm^{-1}$, $^1H$ NMR singlet at $\delta$2.10) and a 2-methylbutyrate ($^1H$ NMR, methyl triplet at $\delta$0.91, methyl doublet at 1.17, methine sextet at 2.39). Deducing the substitution pattern on the sugar came from a detailed analysis of the $^1H$ NMR spectrum of **10**, the alkaline hydrolysis product **11**, and decoupling experiments performed on these compounds. The ester methines of **10** appeared as a complex multiplet at $\delta$4.95. On basic hydrolysis these protons shifted upfield to $\delta$3.41 (proton at C-2′) and 3.55 (proton at C-3′). Assignment of these and all of the ring protons could be made in compound **11** by consideration of chemical shifts and from decoupling data. The relative positions of the acetate and 2-methylbutyrate groups could not be made. The base peak at *m/z* 259 could be assigned to ion **14**. Assignment of the configuration at the anomeric carbon could be made by comparison of the $^{13}C$ NMR resonances in **11** with the methyl glycoside of $\beta$-D-xylopyranoside (Table 4). The assignment made was then $\beta$.

The least polar glycoside (**12**) had a molecular formula of $C_{22}H_{38}O_7$ established by elemental analysis. The highest peak in EI mass spectrum was also *m/z* 259 as in **10**. The $^1H$ NMR and $^{13}C$ NMR spectra of **12** were also very similar to **10**. The major difference was that **12** contained only one carbon double bond. Consideration of these spectra indicated that the 2,3-double bond in the geraniol moiety had been saturated. Catalytic hydrogenation of **12** gave a compound identical to the hydrogenation product of compound **10**.

Table 4. $^{13}C$ NMR spectral data of glycosides **10**, **11** and **12**

| Carbon | 10 | 11* | 12 | | | |
|---|---|---|---|---|---|---|
| 1 | 65.3 *t* | 65.5 *t* | 67.9 | 59.0‡ | | |
| 2 | 119.4 *d* | 121.6 *d* | 37.1 | 124.8 | | |
| 3 | 141.1 *s* | † | 29.4 | 137.6 | | |
| 4 | 39.3 *t* | 40.2 *t* | 36.4 | 40.0 | | |
| 5 | 26.3 *t* | 27.0 *t* | 26.5 | 26.9 | | |
| 6 | 124.5 *d* | 124.8 *d* | 124.6 | 125.2 | | |
| 7 | 131.5 *s* | † | 131.1 | 131.5 | | |
| 8 | 17.5 *q* | 17.6 *q* | 17.6 | 17.7 | | |
| 9 | 25.5 *q* | 25.8 *t* | 25.3 | 25.8 | | |
| 10 | 16.1 *q* | 16.3 *q* | 19.4 | 16.3 | | |
| Xylose | | | | | | |
| 1 | 99.5 *d* | 103.1 *d* | 100.9 | | 105.1§ | |
| 2 | 70.3 *d* | 74.0 *d* | 70.0 | | 74.0 | |
| 3 | 75.5 *d* | 77.0 *d* | 75.5 | | 76.9 | |
| 4 | 68.5 *d* | 70.7 *d* | 68.7 | | 70.4 | |
| 5 | 65.0 *t* | 66.0 *t* | 65.1 | | 66.3 | |
| 2-Methyl butyrate | | | | | | |
| 1 | 175.0 *s* | | 174.9 | | | 176.5‖ |
| 2 | 41.1 *d* | | 41.1 | | | 41.3 |
| 3 | 26.1 *t* | | 25.6 | | | 27.2 |
| 4 | 11.4 *q* | | 11.5 | | | 11.7 |
| 5 | 16.6 *q* | | 16.6 | | | 16.8 |
| Acetate | | | | | | |
| 1 | 171.1 *s* | | 171.5 | | | |
| 2 | 20.7 *q* | | 20.8 | | | |

*Run in acetone-$d_6$.
†Signal not detected.
‡Geraniol, ref. [17].
§Methyl glycoside of $\beta$-D-xylopyranoside, ref. [18].
‖Methyl 2-methylbutyrate, ref. [19].

## EXPERIMENTAL

*Polemonium viscosum* was collected in July 1984 on Red Mountain, MT. The sample was identified by Dr Paul Sawyer, Biology Department, Montana Tech.

IR: $CHCl_3$; $^1H$ NMR, 250 MHz in $CDCl_3$; $^{13}C$ NMR, 62.5 MHz in $CDCl_3$; MS VG 70–70 EHF; mps are uncorr. The fresh plant material was extracted with EtOAc and the extract first separated by CC (silica gel) and further by HPLC (Whatman, M 20) using EtOAc–hexane mixtures as solvents. 1.0 kg of plant material afforded 100 mg of **1**, 350 mg of **2**, 56 mg of **4**, 500 mg of **6**, 20 mg of **8**, 350 mg of **10** and 150 mg of **12**.

19-*Acetoxymanoyl oxide* (**1**). Oil; $[\alpha]_D + 31.5°$($CHCl_3$, *c*0.003); IR $cm^{-1}$ 2930, 2880, 1730, 1220, 1075; $^1H$ NMR $\delta$0.80 (3H, *s*), 0.96 (3H, *s*), 1.26 (6H, *s*), 2.05 (3H, *s*), 3.89 (1H, *d*, *J* = 11.0 Hz), 4.20 (1H, *d*, *J* = 11.0 Hz), 4.93 (1H, *dd*, *J* = 11.0, 1.5 Hz), 5.16 (1H, *dd*, *J* = 17.0, 1.5 Hz), 5.88 (1H, *dd*, *J* = 17.0, 11.0 Hz); MS *m/z* (rel. int.): 333 $[M-Me]^+$ (33), 255 (18), 81 (52), 43 (100); high resolution mass spec, obs. *m/z* 348.2667, $C_{22}H_{36}O_3$ $[M]^+$ requires 348.2670.

*Alkaline hydrolysis of* **1**. Compound **1** (10 mg) was dissolved in MeOH(5 ml) and KOH(10 mg) was added. The reaction was stirred for 24 hr and the solvent removed. $H_2O$ (5 ml) and EtOAc (10 ml) were added, the organic layer separated and dried ($MgSO_4$) and the solvent removed to give a product (8 mg) that was identical to **2**.

19-*Hydroxymanoyl oxide* (**2**). White solid, mp 47–48°; $[\alpha]_D$ + 13.1° ($CHCl_3$, *c*0.013); IR $cm^{-1}$ 3700, 2940, 1460, 1382, 1015; $^1H$ NMR ($CDCl_3$) $\delta$0.80 (3H, *s*), 0.96 (3H, *s*), 1.26 (6H, *s*), 3.45 (1H, *d*, *J* = 11.0 Hz), 3.72 (1H, *d*, *J* = 11.0 Hz), 4.94 (1H, *dd*, *J* = 11.0, 1.5 Hz), 5.16 (1H, *dd*, *J* = 17.0, 1.5 Hz), 5.90 (1H, *dd*, *J* = 17.0, 11.0 Hz); MS *m/z* (rel. int.): 291 $[M-Me]^+$ (58), 177 (39), 81 (72), 43(100); high resolution mass spec, obs *m/z* 306.2557, $C_{20}H_{34}O_2$ $[M]^+$ requires 306.2558.

*Akhdardiol* (**4**). Colourless needles from MeOH–$H_2O$, mp 112–115°; $[\alpha]_D - 12.7°$ ($CHCl_3$, *c*0.013); IR $cm^{-1}$ 3700, 2940, 1465, 1370, 1200, 1010; $^1H$ NMR $\delta$0.98 (6H, *s*), 1.24 (3H, *s*), 3.50 (1H, *d*, *J* = 11.0 Hz), 3.79 (1H, *d*, *J* = 11.0 Hz), 4.83 (1H, *dd*, *J* = 10.0, 1.5 Hz), 4.88 (1H, *dd*, *J* = 15.6, 1.5 Hz), 5.72 (1H, *dd*, *J* = 15.6, 10.0 Hz); MS *m/z* (rel. int.) 306 $[M]^+$: (12), 291 (60), 257 (39), 81 (84), 57 (100), 41 (98); high resolution mass spec, obs *m/z* 306.2560, $C_{20}H_{34}O_2$ $[M]^+$ requires 306.2558.

*Reaction of* **4** *with O-bromobenzoyl chloride*. Compound **4** (50 mg) was dissolved in pyridine (2 ml) and *O*-bromobenzoyl chloride was added (36 mg). The reaction was stirred for 24 hr and the solvent removed to give **5** (68 mg) as a solid. The product was purified by crystallization from MeOH–$H_2O$. Colourless needles, mp 108–109°; IR $cm^{-1}$ 1720; $^1H$ NMR: $\delta$1.05 (3H, *s*), 1.06 (3H, *s*), 1.21 (3H, *s*), 4.15 (1H, *d*, *J* = 11.0 Hz), 4.57 (1H, *d*, *J* = 11.0 Hz), 4.79 (1H, *dd*, *J* = 10.0, 1.5 Hz), 4.85 (1H, *dd*, *J* = 15.6, 1.5 Hz), 4.71 (1H, *dd*, *J* = 15.6, 10.0 Hz), 7.32 (2H, *m*), 7.64 (1H, *m*), 7.77 (1H, *m*); MS *m/z* (rel. int.): 473 $[M-Me]^+$, 470 $[M-H_2O]^+$.

13-*Episclareol* (**6**). Colourless needles from MeOH–$H_2O$, mp 125–127°, $[\alpha]_D + 6.6°$ ($CHCl_3$, *c*0.016); IR $cm^{-1}$ ($CHCl_3$) 3400, 2940, 1465, 1395, 900; $^1H$ NMR ($CDCl_3$) $\delta$0.78 (3H, *s*), 0.79 (3H, *s*), 0.85 (3H, *s*), 1.15 (3H, *s*), 1.25 (3H, *s*), 5.08 (1H, *dd*, *J* = 11.0, 1.5 Hz), 5.25 (1H, *dd*, *J* = 17.0, 1.5 Hz), 5.89 (1H, *dd*, *J* = 17.0,

11.0 Hz); MS *m/z* (rel. int.): 308 $[M]^+$ (2), 293 (5), 290 (20), 199 (70), 81 (90), 43 (100); high resolution mass spec, obs. *m/z* 293.2488, $C_{19}H_{33}O_2$ $[M-Me]^+$ requires 293.2495, obs. *m/z* 290.2611, $C_{20}H_{34}O$ $[M-H_2O]^+$ requires 290.2612.

6,7-*Dimethoxy-5-hydroxyflavone* (**8**). Colourless needles, mp 134–136°; IR $cm^{-1}$ 3700, 3000, 1658, 1490, 1390, 1155; $^1H$ NMR: $\delta$3.95 (3H, *s*), 4.01 (3H, *s*), 6.60 (1H, *s*), 6.70 (1H, *s*), 7.53 (3H, *m*), 7.92 (2H, *m*); MS *m/z* (rel. int.): 298 $[M]^+$ (100), 283 (15), 104 (18); high resolution mass spec. obs. *m/z* 298.0837, $C_{17}H_{14}O_5$ ($M^+$) requires 298.0833.

*Acetylation of* **8**. Compound **8** (10 mg) was dissolved in $Ac_2O$ (2 ml) and pyridine (2 ml) and stirred. After 24 hr the solvents were removed to give **9** (11 mg) as an oil. IR $cm^{-1}$ 1774, 1649; $^1H$ NMR: $\delta$2.47 (3H, *s*), 3.86 (3H, *s*), 3.99 (3H, *s*) 6.60 (1H, *s*), 6.92 (1H, *s*), 7.51 (3H, *m*), 7.86 (2H, *m*); MS *m/z*: 340 $[M]^+$.

3,7-*Dimethyl*-1-[2-O-(2-*methylbutyroyl*)-3-O-*acetyl*-$\beta$-D-*xylopyranosyloxy*]-2,6-*octadiene* (**10**). Oil; $[\alpha]_D-30.8°$ ($CHCl_3$, *c*0.02); IR $cm^{-1}$ 3500, 2950, 1740, 1380, 1030; $^1H$ NMR: $\delta$0.91 (3H, *t*, *J* = 7.0 Hz), 1.17 (3H, *d*, *J* = 7.0 Hz), 1.63 (3H, *brs*), 1.68 (3H, *brs*), 1.71 (3H, *brs*), 2.10 (3H, *s*), 2.39 (1H, *sextet*, *J* = 6.0 Hz), 2.60 (1H, OH), 3.34 (1H, *dd*, *J* = 11.5, 9.7 Hz), 3.85 (1H, *m*), 4.10 (1H, *dd*, *J* = 11.5, 5.1 Hz), 4.18 (1H, *dd*, *J* = 10.5, 6.0 Hz), 4.24 (1H, *dd*, *J* = 10.5, 6.1 Hz), 4.47 (1H, *d*, *J* = 6.8 Hz), 4.95 (2H, *m*), 5.10 (1H, *brt*, *J* = 7.0 Hz), 5.25 (1H, *brt*, *J* = 7.0 Hz); MS *m/z* (rel. int.): 259 $[M-C_{10}H_{17}O]^+$ (11), 199 (28), 85 (70), 69 (100), 57 (92). (Anal. Calc for $C_{22}H_{36}O_7$: C, 64.08; H, 8.74 Found C, 63.94; H, 8.77%).

*Hydrogenation of* **10**. Compound **10** (10 mg) was dissolved in MeOH (10 ml) and a pinch of 10% Pd/C added. The reaction was stirred under $H_2$ for 2 hr. After that time the catalyst was filtered off and the solvent removed to yield a product identical to **13** (10 mg)

*Alkaline hydrolysis of* **10**. Compound **10** (20 mg) was dissolved in MeOH (10 ml) and KOH (20 mg) added. The mixture was stirred for 2 hr, the solvent removed and the residue dissolved in EtOAc (10 ml) and $H_2O$ (10 ml). The organic layer was separated, dried ($MgSO_4$) and the solvent removed to give **11** (10 mg) as an oil. $^1H$ NMR (acetone-$d_6$): $\delta$1.59 (3H, *brs*), 1.65 (6H, *brs*), 3.31 (1H, *dd*, *J* = 11.0, 8.1 Hz), 3.41 (1H, *brt*, *J* = 5.8 Hz), 3.55 (1H, *brt*, *J* = 5.8 Hz), 3.71 (1H, *m*), 4.01 (1H, *dd*, *J* = 11.0, 3.8 Hz), 4.12 (1H, *dd*, *J* = 11.0, 7.2 Hz), 4.29 (1H, *dd*, *J* = 11.0, 6.2 Hz), 4.37 (1H, *d*, *J* = 5.8 Hz), 5.05 (1H, *brt*, *J* = 7.0 Hz), 5.31 (1H, *brt*, *J* = 7.0 Hz).

*Acid hydrolysis of* **10**. Compound **10** (20 mg) was dissolved in MeOH (10 ml) and 1 drop of conc HCl added. The mixture was stirred for 24 hr. After that time the solvent was removed, the residue dissolved in EtOAc (10 ml) and $H_2O$ (10 ml), the $H_2O$ layer separated and the solvent removed to yield 6 mg of a white solid. The solid proved to be identical to to xylose $[\alpha]_D$ by TLC in three different solvent systems. The organic layer was dried and removed to yield 2 mg of an oil which was shown to be geraniol by GC-MS.

3,7-*Dimethyl*-1-[2-O-(2-*methylbutyroyl*)-3-O-*acetyl*-$\beta$-D-*xylopyranosyloxy*]-6-*octene* (**12**). Oil; $[\alpha]_D-0.15°$ ($CHCl_3$, *c*0.02); IR $cm^{-1}$ 3600, 2940, 1740, 1375, 1040; $^1H$ NMR: $\delta$0.89 (3H, *t*, *J* = 7.0 Hz), .90 (3H, *d*, *J* = 7.0 Hz), 1.15 (3H, *d*, *J* = 7.0 Hz), 1.60 (3H, *br s*), 1.70 (3H, *br s*), 2.10 (3H, *s*), 2.40 (1H, *sextet*, *J* = 6.0 Hz), 2.58 (1H, OH), 3.34 (1H, *dd*, *J* = 11.5, 9.7 Hz), 3.51 (1H, *m*), 3.85 (2H, *m*), 4.10 (1H, *dd*, *J* = 11.4, 5.1 Hz), 4.47 (1H, *d*, *J* = 6.8 Hz), 4.95 (2H, *m*), 5.10 (1H, *brt*, *J* = 7.0 Hz); MS *m/z* (rel. int.): 259 $[M-C_{10}H_{19}O]^+$ (17), 199 (50), 85 (89), 57 (100). (Anal. Calc for $C_{22}H_{38}O_7$: C, 63.77; H, 9.18. Found: C, 63.47; H, 9.20%).

*Hydrogenation of* **12**. Compound **12** (10 mg) was dissolved in MeOH (10 ml) and a pinch of 10% Pd/C added. The reaction was stirred under $H_2$ for 2 hr. After that time the catalyst was filtered off and the solvent removed to yield **13** (10 mg) as an oil. $^1H$ NMR: $\delta$0.85 (9H, *m*), 1.11 (3H, *d*, *J* = 7.0 Hz), 2.05 (3H, *s*), 3.32 (1H, *dd*, *J* = 11.5, 9.6 Hz), 3.45 (1H, *m*), 3.81 (2H, *m*), 4.06 (1H, *dd*, *J* = 11.5, 4.8 Hz), 4.40 (1H, *br d*), 4.91 (2H, *m*); MS *m/z* (rel. int.): 259 $[M-C_{10}H_{21}O]^+$ (4), 199 (10), 85 (98), 57 (100).

*X-ray structure determination of* **5**. A suitable crystal (1.46 × 0.20 × 0.16 mm, colourless) of **5** was grown from MeOH–$H_2O$ and mounted on a glass fibre. Axial photographs showed orthorhombic symmetry. Unit cell dimensions were obtained by least-squares refinement using 25 centered reflections for which $19° < 2\theta < 24°$ (graphite monochromatized MoK$\alpha$, $\lambda$ = 0.71069 Å). Intensity data were collected at $\theta/2\theta$ scans on Nicolet R3m/E four circle diffractometer with three check reflections monitored at intervals of 100 reflections. Systematic extinctions indicated space group $P2_12_12_1$. Other crystal data are: $C_{27}H_{37}O_3Br$, $Z = 4$, $a = 7.390(1)$, $b = 16.177(4)$, $c = 20.635(4)$ Å, V = 2467(1) Å$^3$, $d_{calc} = 1.32$ g/cm$^3$, (MoK$\alpha$) = 16.72 $cm^{-1}$. Intensities were measured for 4077 reflections in the range $3° < 2\theta < 60°$ (th, + K, + 1) with 1470 considered observed by the criterion $I > 2\sigma(I)$. The data were corrected for Lorentz and polarization effects [20]; absorption corrections were calculated by the Gaussian integration method (transmission range: 0.67–0.78). A Patterson synthesis gave the bromine position and the remaining atoms were located by $F_o$-$F_c$ difference maps. Positions were refined with anisotropic thermal parameters by blocked cascade least-squares, minimizing $\Sigma W(|F_o|-|F_c|)^2$, with $W = [\sigma^2(F_o)+.0003\ (F_o)^2]^{-1}$. Atomic scattering factors, including anomalous scattering, were taken from Cromer and Waber [21]. Three reflections showing strong extinction effects were excluded from the final refinement cycles. All hydrogen atoms were found in difference maps, but calculated positions were used in refinement with common isotopic temperature factors refined for primary, secondary, and aromatic hydrogens, respectively. The refinement behaviour of C(15) and an addition peak on difference maps indicated partial disorder of the C(15) position. In the final stages of refinement this disorder was modeled with two positions for C(15). The predominate position (85%, shown in Fig. 1) was refined anisotropically and the minor position isotropically. Positional coordinates for C(15) and C(15′) were refined under constraints to give idealized bond distances to C(14). Rather large refined thermal parameters for C(15) and C(15′) suggest that the two position disorder model is overly simplified. Refinement of a parameter, $\eta$, multiplying $\Delta f''$ terms [22] indicated absolute configuration to be that shown in Fig. 1 [$\eta = 0.92(5)$]. Refinement of the inverted structure leads to significantly higher *R* values, confirming absolute configuration. Final refinement statistics: 292 parameters, $R = 0.069$, $R_w = 0.057$, goodness of fit = 1.68. (Inverted structure: $R = 0.081$, $R_w = 0.071$.) A list of observed and calculated structure factors, atomic coordinates, bond lengths and angles, anisotropic thermal parameters, and calculated hydrogen atom positions have been deposited at the Cambridge Crystallographic Centre.

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