Phytochemistry, Vol. 27, No. 10, pp. 3273–3275, 1988.
Printed in Great Britain.

0031 9422/88 $3.00+0.00
Pergamon Press plc.

PRENYL FLAVANES FROM *MARSHALLIA* SPECIES

J. JAKUPOVIC, L. PAREDES, F. BOHLMANN and L. WATSON*

Institute of Organic Chemistry, Technical University of Berlin, D-1000 Berlin 12, F.R.G.; *Department of Botany, University of Oklahoma, Norman, Oklahoma 73019, U.S.A.

(*Received in revised form* 14 *March* 1988)

Key Word Index—*Marshallia mohrii, M. grandiflora, M. tenuifolia, M. trinervia, M. ramosa, M. graminifolia*; prenyl flavanes; glycosides; prenyl flavanone; inositol esters.

Abstract—The aerial parts of *Marshallia mohrii* afforded three new prenylated flavane glycosides. From *M. tenuifolia* in addition to known flavanes and an inositol ester, two new ones were isolated. *Marshallia grandiflora* gave a further prenylated flavanone and three further *Marshallia* species gave only known flavanes. The structures were elucidated by high field NMR spectroscopy.

INTRODUCTION

So far three species of the genus *Marshallia* have been studied chemically, they all gave prenylated flavanes and from two species inositol esterified with unsaturated esters were reported [1–3]. As this genus shows no clear relationships to other groups, its position is still in question. It has been excluded from the Heliantheae [4] and its placement in the Eupatorieae has been discussed [5]. Recently, it has been assigned to a monogeneric subtribe Marshalliinae of the Heliantheae [6]. We have studied four species and reinvestigated two others, the results are discussed in this paper.

RESULTS AND DISCUSSION

The investigation of the aerial parts of *M. mohrii* Beadle et Boynt., *M. tenuifolia* Raf., *M. ramosa* Beadle et Boynt., *M. graminifolia* (Walt.) Small., *M. grandiflora* Beadle et Boynt. and *M. trinervia* (Walt.) Trel. afforded in all cases prenylated flavanes (see Experimental). In addition to known compounds three flavane glycosides (**3**–**5**), a prenylated flavanone (**7**), the inositol ester **8** [1] and two further ones (**9** and **10**) were isolated.

The ^{1}H NMR spectra of **3** and **4** (Table 1) indicated that glycosides of **1** and **2** respectively, were present. Spin decoupling showed that the signals of the sugar moiety required a β-glucopyranoside. The relative position of the oxygen functions could be determined by NOE difference spectroscopy. Clear effects were observed between methoxy and H-6, between H-4, H-3 and methoxy as well as between H-1 of the glucoside, H-6, H-1″ and H-2″. The stereochemistry at C-2–C-4 followed from the couplings. The proposed absolute configuration is that of the corresponding flavane derivative [1].

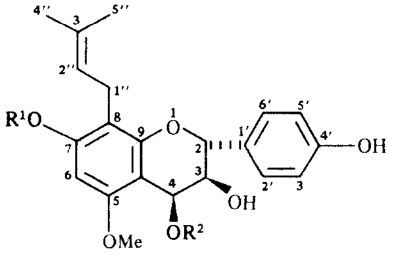
The ^{1}H NMR spectrum of **5** indicated the presence of a disaccharide moiety. Acetylation gave the nonaacetate **5a**. Its ^{1}H NMR spectrum (Table 1) could be fully assigned by spin decoupling in deuterio pyridine. The chemical shifts and couplings of the sugar moiety only agreed with a β-xylopyranosyl-(1→6)-β-glucopyranoside and the relative position of the sugar moiety was deduced from the observed NOE between H-1 of the glucoside and H-2 of the flavane. As the chemical shift of H-3 clearly indicated that an acetoxy group was at this centre the sugar moiety only could be placed at the 4-hydroxy group of the flavane **1**. Again the stereochemistry followed from the observed couplings.

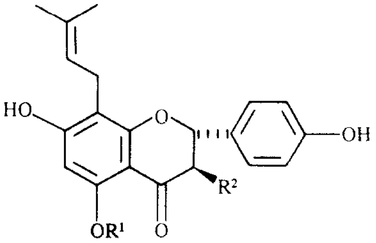
Table 1. ^{1}H NMR spectral data of compounds **3**, **4** and **5a** (400 MHz, $CDCl_3$, δ-values)

H	**3** (MeOD)	**4**	**5a** (pyridine-d_5)*
2	4.90 *d*	4.92 *d*	5.69 *d*
3	3.75 *dd*	3.80 *dd*	5.51 *dd*
4	4.95 *d*	4.61 *d*	5.50 *d*
6	6.53 *s*	6.47 *s*	6.73 *s*
2′,6′	7.28 *br d*	7.26 *br d*	7.65 *br d*
3′,5′	6.80 *br d*	6.78 *br d*	7.32 *br d*
1″	3.33 *br dd* 3.15 *br dd*	3.31 *br dd* 3.15 *br dd*	3.33 *br dd* 3.15 *br dd*
2″	5.13 *br t*	5.10 *br t*	5.33 *br t*
4″	1.57 *br s*	1.56 *br s*	1.58 *br s*
5″	1.48 *br s*	1.45 *br s*	1.55 *br s*
OGluc			
1	4.90 *d*	4.84 *d*	5.74 *d*
2	3.40 *m*	3.51 *dd*	5.78 *dd*
3		3.40 *m*	5.86 *t*
4			5.59 *t*
5			4.44 *ddd*
6	3.91 *dd*	3.90 *dd*	4.56 *dd*
6′	3.67 *dd*	3.69 *dd*	4.52 *dd*
OMe	3.83 *s*	3.81 *s* 3.53 *s*	3.90 *s*

*Xyloside: H-1 5.29 *d*, H-2 5.47 *dd*, H-3 5.68 *t*, H-4 5.23 *ddd*, H-5_1 3.67 *dd*, H-5_2 4.28 *dd*; OAc: 1.90, 1.94, 1.99, 2.03, 2.04 (2 ×), 2.15, 2.19 (2 ×) *s*.

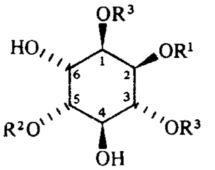
J[Hz]: 2,3 = 10; 3,4 = 3.5; 2′,3′ = 8; $1''_1,1''_2 = 14$; $1''_1,2'' = 7$; OGluc: 1,2 = 2,3 = 3,4 = 4,5 ~ 9; 5,6_1 = 5; 5,6_2 = 2.5; 6_1,6_2 = 12.





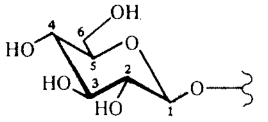
	1	2	3	4	5
R^1	H	H	Gluc*	Gluc*	H
R^2	H	Me	H	Me	Gluc-Xyl†

	6	7
R^1	H	Me
R^2	H	OH

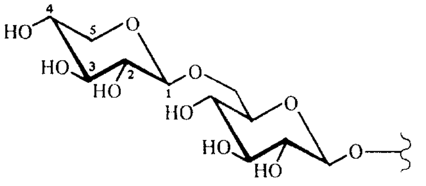


	8	9	10
R^1	H	Mesen	2 x Mesen
R^2	Ang	Mesen	1 x Ang
R^3	Ang	H	H

*Gluc =



†Gluc-Xyl =



5a is the corresponding nonaacetate

The ¹H NMR data of **7** (see Experimental) were close to those of **6** [2]. The presence of a 3β-hydroxy and a 5-methoxy group followed from the corresponding ¹H NMR signals. A NOE between the methoxy group and H-6 indicated the C-8 position of the prenyl group while the absence of a hydrogen bond showed that the methoxy group was at C-5.

The ¹H NMR spectra of **9** and **10** (Table 2) were similar. The couplings clearly indicated that triesters of inositol were present. From the chemical shifts the relative position of the oxygen functions could be deduced. However, in the case of **10** the position of the angelate residue could not be determined. In three species the mixtures of inositol esters could not be separated but their presence clearly followed from the typical splitting of the inositol proton signals.

The new results again showed that prenylated flavanes and esters of inositol are typical for the genus *Marshallia*. However, relationships to other genera are still not very clear. Prenylated flavanones have been reported from *Wyethia* [7, 8] and *Flourensia* [9] (Heliantheae) and from *Helichrysum* [10] which may indicate that *Marshallia* is an intermediate between the tribes Heliantheae and Inuleae.

EXPERIMENTAL

The air-dried aerial parts (vouchers deposited in the University of Oklahoma, except for *M. grandiflora*, deposited in the Smithsonian Institution, Washington) were extracted with MeOH–Et_2O–petrol (1:1:1) and the extracts obtained were worked-up and separated as reported previously [11]. Final separation required HPLC (RP 8, MeOH–H_2O, *ca* 100 bar) and the R_t values of the new compounds are given below.

Marshallia graminifolia (50 g, voucher LW 687, collected August 1987, Georgia, North Carolina, South of Havelock) gave 15 mg **1** [3], 30 mg **2** [3] and 35 mg inositol esters. *M. grandiflora*

Table 2. ^{1}H NMR spectral data of compounds **9** and **10** (400 MHz, $CDCl_3$, δ-values)

H	**9**	**10**
1	4.25 *br s*	4.25 *br s*
2	4.25 *br s*	4.25 *br s*
3	5.40 *dd*	5.45 *dd*
4	5.46 *t*	5.53 *t*
5	4.10 *ddd*	4.13 *ddd*
6	5.32 *dd*	5.34 *dd*
OH	2.41 *d*	2.44 *d*
OCOR	5.75, 5.66 (2 ×) *br s*	6.03 *qq*
	2.13 *dq*	1.93 *dq*
	2.18, 2.16, 2.14 *d*	1.85 *dq*
	1.08, 1.05, 1.04 *t*	2.20 *br q*
		5.76, 5.67 *br s*
		2.19, 2.15 *d*
		1.09, 1.06 *t*

J[Hz]: 2,3 = 2; 3,4 = 4,5 = 10; 5,6 = 2; 5, OH = 6.5; OMeSen: 2,6 = 1.5; 4,5 = 7; OAng: 3,4 = 7; 3,5 = 4,5 = 1.5.

(250 g, voucher RMK 1551, collected September 1978, West Virginia, Randolph County by E. E. Hutton jr., Elking, West Virginia) gave 15 mg **1** [3], 40 mg **2** [3] and 5 mg **7**. *M. mohrii* (32 g, voucher LW 629, collected June 1982, Alabama, South of Centre on ALA9) gave 2 mg **3**, 20 mg **4**, 25 mg **5** and 30 mg cyclo **6** [2]. *M. ramosa* (30 g, voucher LW 699, collected August 1987, Georgia, near Oknulgee River) gave 20 mg **1** [3], 10 mg **2** [3] and 20 mg inositol ester. *M. tenuifolia* (33 g, voucher LW 614, collected August 1985, Louisiana, Kisatchie National Forest) gave 20 mg **2** [3], 15 mg **6** [3], 50 mg **8** [1], 30 mg **9** and 20 mg **10**. *M. trinerva* (50 g, voucher LW 641, collected June 1986, Alabama, N of Deev Park, state highway ALA9) gave 20 mg **2** [3] and 30 mg inositol esters. Known compounds were identified by comparing the 400 MHz ^{1}H NMR spectra with those of authentic material.

3β,4β,7,4′-*Tetrahydroxy*-5-*methoxy*-8-[3,3-*dimethyl allyl*] *flavane*-7-O-β-D-*glucopyranoside* **(3)**. HPLC (MeOH–H_2O, 2:3, R_t 11.9 min); colourless gum; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3400 (OH); MS *m/z* (rel. int.): 398 $[M-HOCH{=}CHC_6H_4OH]^+$ (2), 236 (24), 221 (14), 181 (28), 107 $[C_7H_6OH]^+$ (100); $[\alpha]_D^{24°}$ −13.5° (MeOH; *c* 0.15).

3β,7,4′-*Trihydroxy*-4β,5-*dimethoxy*-8-[3,3-*dimethyl allyl*] *flavane*-7-O-β-D-*glucopyranoside* **(4)**. HPLC (MeOH–H_2O, 2:3, R_t 7.6 min); colourless gum; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3400 (OH); MS *m/z* (rel. int.): 548.227 $[M]^+$ (2) (calc. for $C_{28}H_{36}O_{11}$: 548.226), 386 $[M-\text{glucosyl}]^+$ (6), 354 $[386-MeOH]^+$ (24), 107 (100); $[\alpha]_D^{24°}$ −20.5° (MeOH; *c* 0.8).

3β,4β,7,4′-*Tetrahydroxy*-5-*methyl*-8-[3,3-*dimethyl allyl*] *flavane*-4-O-[β-D-*xylopyranosyl*-(1→6)]-β-D-*glucopyranoside* **(5)**. HPLC (MeOH–H_2O, 2:3, R_t 13.9 min); colourless gum; MS *m/z* (rel. int.): 354 $[M-\text{glycoside}]^+$ (44), 248 $[354-C_7H_6O]^+$ (52), 107 $[C_7H_6OH]^+$ (100). It was transformed to the nonaacetate **5a** by reaction of **5** with DMAP–Ac_2O in $CDCl_3$; colourless crystals, mp. 190–194°; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1740 (OAc); $[\alpha]_D^{24°}$ −12° ($CHCl_3$; *c* 0.33); ^{13}C NMR (MeOD, C-2–C-10): δ78.4, 72.3, 78.4, 158.6, 93.0, 158.5, 111.9, 158.5, 106.8; C-1′–C-6′: δ131.0, 130.3, 115.9, 154.3, 115.9, 130.3; C-1″–C-5″: 22.9, 124.2, 131.3, 26.0, 18.0; Gluc C-1–C-6: 106.7, 75.1, 78.0, 71.1, 77.8, 62.8; xyl C-1–C-5: 102.9, 74.2, 75.8, 71.7, 63.3; OMe: 56.1 (some signals may be interchangeable).

3β,7,4′-*Trihydroxy*-5-*methoxy*-8-[3,3-*dimethyl allyl*] *flavanone* **(7)**. TLC (Et_2O–petrol, 3:1, R_f 0.35); colourless oil. CIMS *m/z* (rel. int.): 371 $[M+1]^+$ (42), 356 $[371-Me]^+$ (32), 238 (64), 237 (100), 165 (77), 123 (98), 107 (70); ^{1}H NMR ($CDCl_3$–CD_3OD): 5.08 (*d*, 2-H), 4.06 (*d*, 3-H), 5.68 (*s*, 6-H), 3.04 and 2.96 (*br dd*, 1″-H), 5.01 (*br t*, 2″-H), 1.59 and 1.48 (*br s*, 4″-H, 5″-H), 7.17 (*d*, 2′-H, 6′-H), 6.82 (*d*, 3′-H, 5′-H); OMe: 3.72 *s*; (*J* [Hz]: 2,3 = 9.5; $1''_1$, $1''_2$ = 14; 1″, 2″ = 7; 2′,3′ = 8.5).

2,4,5-*Trimethylsenecioyl inositol* **(9)**. HPLC (MeOH–H_2O, 13:7, R_t 23.5 min); colourless oil; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3600 (OH), 1720 ($C{=}CCO_2R$); MS *m/z* (rel. int.): 468.236 $[M]^+$ (0.7) (calc. for $C_{24}H_{36}O_9$: 468.236), 450 $[M-H_2O]^+$ (1), 355 $[M-OCOR]^+$ (1.7), 354 $[M-RCO_2H]^+$ (2), 240 $[354-RCO_2H]^+$ (1), 126 $[240-RCO_2H]^+$ (6), 97 $[RCO]^+$ (100).

2,4,5-*Dimethylsenecioyl and angeloyl inositol* **(10)**. HPLC (MeOH–H_2O, 13:7, R_t 12.4 min); colourless oil; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3580 (OH), 1720 ($C{=}CCO_2R$); MS *m/z* (rel. int.): 454.220 $[M]^+$ (3) (calc. for $C_{23}H_{34}O_9$: 454.220), 436 $[M-H_2O]^+$ (3.5), 355 $[M-OAng]^+$ (2.5), 340 $[M-MeSenOH]^+$ (4), 240 $[340-AngOH]^+$ (0.5), 126 $[240-RCO_2H]^+$ (5), 97 $[RCO]^+$ (100), 83 $[RCO]^+$ (28); $[\alpha]_D^{24°}$ −27° ($CHCl_3$; *c* 1.0).

Acknowledgements—We thank Dr E. E. Hutton (West Virginia) and Dr R. M. King (Washington) for plant material.

REFERENCES

1. Herz, W. and Bruno, M. (1987) *Phytochemistry* **26**, 1175.
2. Bohlmann, F., Jakupovic, J., King, R. M. and Robinson, H. (1980) *Phytochemistry* **19**, 1815.
3. Bohlmann, F., Zdero, C., King, R. M. and Robinson, H. (1979) *Phytochemistry* **18**, 1246.
4. Stuessy, T. F. (1977) *The Biology and Chemistry of the Compositae* (Heywood, V. H., Harborne, J. B. and Turner, B. L., eds), p. 654. Academic Press, London.
5. Turner, B. L. and Powell, A. M. (1977) *The Biology and Chemistry of the Compositae* (Heywood, V. G., Harborne, J. B. and Turner, B. L., eds), pp. 713, 716. Academic Press, London.
6. Robinson, H. (1981) *Smithsonian Contr. Botany* **51**, 88.
7. Bohlmann, F., Zdero, C., Robinson, H. and King, R. M. (1981) *Phytochemistry* **20**, 2245.
8. McCormick, S., Robson, K. and Bohm, B. (1986) *Phytochemistry* **25**, 1723.
9. Bohlmann, F., Jakupovic, J., Schuster, A., King, R. M. and Robinson, H. (1984) *Phytochemistry* **23**, 1445.
10. Bohlmann, F. and Zdero, C. (1983) *Phytochemistry* **22**, 2877.
11. Bohlmann, F., Zdero, C., King, R. M. and Robinson, H. (1984) *Phytochemistry* **23**, 1979.