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A DITERPENE, A SESQUITERPENE QUINONE AND FLAVANONES FROM *WYETHIA HELENIOIDES**

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Key Word Index—*Wyethia helenioides*; Compositae; geranylnerol derivative; prenylated flavanones; bisabolene derivatives.

Abstract—The aerial parts of *Wyethia helenioides* afforded a new geranyl nerol derivative (a 16-hydroxy-18-oic acid), two isomeric prenylated flavanones and a quinone derived from bisabolene. The structures were elucidated by spectroscopic methods and some chemical transformations. The chemotaxonomic situation is discussed briefly.

INTRODUCTION

The genus *Wyethia* is placed in the tribe Heliantheae, subtribe Helianthinae [1]. So far little is known on the chemistry of this genus, most species of which are distributed in the western part of North America. From the roots of one species the widespread trideca-pentaynene was isolated [2]. We have now investigated the aerial parts of *Wyethia helenioides* (DC) Nutt. In addition to known compounds, a new geranylnerol derivative, prenylated flavanones and a quinone derived from bisabolene were isolated.

RESULTS AND DISCUSSION

The aerial parts of *W. helenioides* afforded germacrene D, caryophyllene and its epoxide, sitosterol, stigmasterol, the isoflavones santal (**13**) [3] and 3′-methylorobol (**14**) [4] and three prenylated flavanones, only one of which was known (**1**) [5]. The structures of the two other flavanones (**2** and **3**) followed from their ^{1}H NMR data (Table 1) and from those of **4**–**6** obtained by acid-catalysed ring closure. The ^{1}H NMR data of **2** and **3** clearly showed that they were flavanones with hydroxyls at C-5, C-7, C-3′ and C-4′, while the position of the prenyl residues could not be assigned

Table 1. ^{1}H NMR spectral data of compounds **2**–**6** ($CDCl_3$, 400 MHz, TMS as internal standard)

	2*	**3**	**3***	**4**	**5**	**6**
2-H	5.39 *dd*	5.30 *dd*	5.38 *dd*	5.26 *dd*	5.32 *dd*	5.33 *dd*
3-H	3.12 *dd*	3.01 *dd*	3.09 *dd*	3.02 *dd*	2.99 *dd*	3.00 *dd*
3′-H	2.69 *dd*	2.78 *dd*	2.73 *dd*	2.76 *dd*	2.77 *dd*	2.77 *dd*
6-H	6.02 *s*	—	—	5.92 *s*	—	—
8-H	—	6.01 *s*	6.02 *s*	—	2.93 *s*	5.97 *s*
2′-H	7.02 *s* (*br*)	6.98 *d*	7.04 *d*	6.98 *s* (*br*)	6.99 *d*	7.02 *d*
5′-H	6.85 *s* (*br*)	6.89 *d*	6.85 *d*	6.89 *d*	6.90 *d*	6.92 *d*
6′-H		6.86 *dd*	6.88 *dd*	6.86 *d* (*br*)	6.87 *dd*	6.89 *dd*
1″-H	3.23 *d*	3.31 *d* (*br*)	3.21 *d* (*br*)	2.61 *t*	2.62 *t*	2.59 *t*
2″-H	5.22 *t* (*br*)	5.20 *t* (*br*)	5.18 *t* (*br*)	1.78 *t*	1.79 *t*	1.75 *t*
4″-H	1.74 *s* (*br*)	1.73 *s* (*br*)	1.61 *s* (*br*)	1.34 *s*	1.33 *s*	1.34 *s*
5″-H	1.63 *s* (*br*)	1.73 *s* (*br*)	1.61 *s* (*br*)	1.33 *s*	1.34 *s*	1.32 *s*
OH	12.47 *s*	11.98 *s*	12.13 *s* 8.01 *s*	12.37 *s*	12.34 *s*	11.74 *s*

J (Hz): 2,3 = 12.5; 2,3′ = 3; 3,3′ = 17; 1′,6′ = 1.5; 5′,6′ = 8; 1″,2″ = 7.
*C_3D_6O.

*Part 357 in the series "Naturally Occurring Terpene Derivatives". For Part 356 see Bohlmann, F., Jakupovic, J., Abraham, W.-R. and Zdero, C. (1981) *Phytochemistry* **20** (in press).

directly. However, heating of **2** and **3** in benzene with toluene sulfonic acid afforded the isomeric dihydro chromenes **4**, and **5** and **6** respectively. This established that the prenyl residue of **3** was at C-6 and that that of **2** was at C-8. When the data of **2** and **3** were compared, it was obvious that the position of the prenyl group influenced the chemical shift of the bonded OH–proton. In compound **2**, the corresponding signal was shifted more downfield as in the spectrum of **3**. Also the shifts of one of the olefinic methyls was shifted upfield in **3**, while the chemical shifts of H-6 and H-8 respectively were nearly identical. These observations may be useful in the characterization of similar compounds.

From the less polar fractions a yellow oil (**7**) was isolated, which on reaction with sodium borohydride afforded the hydroquinone **8**. The structure of the natural compound (**7**) followed from the ^{1}H NMR data (Table 2). The absence of a *meta* coupling in the signals of the aromatic protons of **8** excluded a 1,6-disubstituted hydroquinone. **7**, therefore, is 6-deoxyperezone. Though the absolute configuration was not determined, the proposed one was very likely as the optical rotation of **8** had the same sign as those of other aromatic bisabolene derivatives with known stereochemistry.

The most polar fractions contained in high concentration a diterpenic acid. The ^{1}H NMR data (Table 3) showed that a geranyl nerol derivative was present with one additional hydroxy group and one methyl being transformed to a carboxyl group. The structure and the stereochemistry (**9**), however, could be deduced only from the ^{1}H NMR data of the dialdehyde **11** obtained after addition of diazomethane and manganese dioxide oxidation. Spin decoupling allowed the assignment of all signals (Table 3). The chemical shifts of H-1 and H-20 led to the configuration of the 2,3-double bond, while the shift of H-14 confirmed that of the 14,15-double bond. The position of the ester group was also deduced from the result of spin decoupling. H-12 was assigned from decoupling of the H-13 signal, which was coupled with the downfield shifted olefinic proton at C-14. Irradiation of H-12 sharpened the H-10 signal. This proton, however, had to be placed β to the ester carbonyl as the chemical shift of the corresponding signal was nearly unchanged in all derivatives (**9**–**12**). **9** we have named wyethic acid.

Table 2. ^{1}H NMR spectral data of compounds **7** and **8** ($CDCl_3$, 400 MHz, TMS as internal standard)

	7	**8**
3-H	6.58 *q*	6.57 *s* (*br*)
6-H	6.50 *d*	6.55 *s* (*br*)
7-H	2.90[5] *tq*	2.93 *tq*
8-H	1.44 *m*	1.58 *m*
9-H	1.95 *dt*	1.92 *dt*
10-H	5.04 *t* (*br*)	5.11 *t* (*br*)
12-H	1.65 *s* (*br*)	1.67 *s* (*br*)
13-H	1.54 *s* (*br*)	1.63 *s* (*br*)
14-H	1.10 *d*	1.18 *d*
15-H	2.03 *d*	2.16 *s*

J (Hz): compound **7**: 3,15 = 1.5; 6,7 = 2; 7,14 = 7; 7,8 = 7; 8,9 = 7; 9,10 = 7; compound **8**: 7,8 = 7; 7,14 = 7; 8,9 = 7; 9,10 = 7.

Table 3. ^{1}H NMR spectral data of compounds **9**–**12** ($CDCl_3$, 400 MHz, TMS as internal standard)

	9	**10**	**11**	**12**
H-1	4.09 *d* (*br*)	4.10 *d* (*br*)	9.88 *d*	4.56 *d* (*br*)
H-2	5.38 *t* (*br*)	5.42 *t* (*br*)	5.83 *d* (*br*)	5.37 *t* (*br*)
H-4	2.06 *s* (*br*)	2.09 *s* (*br*)	2.57 *t* (*br*)	2.10 *s* (*br*)
H-5			2.24 *dt* (*br*)	
H-6	5.07 *t* (*br*)	5.12 *t* (*br*)	5.10 *t* (*br*)	5.12 *t* (*br*)
H-8	2.03 *t* (*br*)	2.06 *t* (*br*)	2.03 *t* (*br*)	2.05 *t* (*br*)
H-9	2.51 *dt* (*br*)	2.49 *dt* (*br*)	2.51 *dt* (*br*)	2.60 *dt* (*br*)
H-10	5.83 *t* (*br*)	5.84 *t* (*br*)	5.87 *t* (*br*)	6.01 *t*
H-12	2.27 *t* (*br*)	2.28 *t* (*br*)	2.39 *t* (*br*)	2.23 *t* (*br*)
H-13	2.17 *dt* (*br*)	2.16 *dt* (*br*)	2.67 *dt* (*br*)	2.28 *dt* (*br*)
H-14	5.24 *t* (*br*)	5.23 *t* (*br*)	6.46 *t* (*br*)	5.35 *t* (*br*)
H-16	4.05 *s* (*br*)	4.05 *s* (*br*)	10.04 *s*	4.57 *s* (*br*)
H-17	1.69 *s* (*br*)	1.73 *s* (*br*)	1.73 *dt*	1.73 *s* (*br*)
H-19	1.56 *s* (*br*)	1.59 *s* (*br*)	1.57 *s* (*br*)	1.60 *s* (*br*)
H-20	1.75 *s* (*br*)	1.78 *s* (*br*)	1.96 *d*	1.76 *s* (*br*)
OMe	—	3.73 *s*	3.72 *s*	—
OAc				2.05 *s*
				2.04 *s*

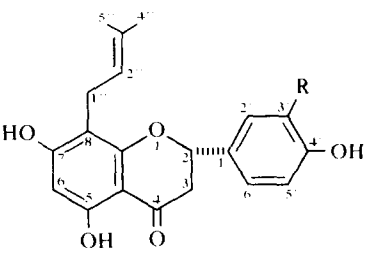
J (Hz): compounds **9**, **10** and **12**: 1,2 = 5,6 = 8,9 = 9,10 = 13,14 = 7; compound **11**: 1,2 = 8; 4,5 = 7.5; 8,9 = 9,10 = 7; 12,13 = 7.5; 13,14 = 8.5; 13,17 = 14,17 = 1.

The isolation of **1**–**3** may be of chemotaxonomic importance in relation to the position of the genus *Marshallia*, where similar prenylated flavanones and flavanes are characteristic [5,6]. The taxonomic value of geranyl nerol derivatives is still in question as the distribution of these compounds is not really well known, though already 17 diterpenes of this type have been isolated from many genera, all belonging to the Heliantheae (*Acanthospermum* [7], *Aspilia* (F. Bohlman, unpublished work), *Dimerostemma* [8], *Kingianthus* [9], *Montanoa* [10], *Zinnia* [11]) and Eupatorieae (*Bejaronoa* [12], *Grazielia* [13], *Lasiolaena* [14], *Liatris* [15], *Koanophyllon* [16], *Mikania* [F. Bohlman, unpublished work], *Stylotrichium* [17]).

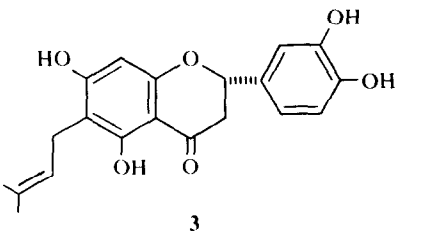
EXPERIMENTAL

The air-dried aerial parts (600 g) (voucher RMK 8421) were extracted with Et_2O–petrol (1:2) and the resulting extract after treatment with MeOH to remove long-chain hydrocarbons was first separated by CC (Si gel) and further by repeated TLC (Si gel). Known compounds were identified by comparing their IR and ^{1}H NMR spectra with those of authentic material. Finally, 10 mg caryophyllene and 10 mg of its epoxide, 5 mg germacrene D, 50 mg sitosterol, 50 mg stigmasterol, 11 mg **7** (Et_2O–petrol, 1:10), 500 mg of a mixture of **1**–**3**, **13** and **14** of wich only 100 mg were sepd, first by TLC and further by HPLC (reversed phase, RP 2, MeOH–H_2O, 3:2). The fractions obtained with Et_2O–MeOH (20:1) afforded 600 mg **9**.

5,7,3′,4′-Tetrahydroxy-8-[3′,3′-dimethylallyl]-flavanone (**2**). Colourless crystals, mp 189° ($CHCl_3$), IR ν_{max}^{KBr} cm^{-1}: 3410 (OH), 1645, 1610 (PhCO); MS *m/z* (rel. int.): 356.126 (M^+, 100) ($C_{20}H_{20}O_6$), 341 (M – Me, 18), 313 (M – C_3H_7, 15), 301 (M – C_4H_7, 22), 165 (301 – $C_8H_8O_2$, 80). 3 mg **2** in 2 ml C_6H_6 were heated with 5 mg *p*-toluene sulfonic acid for 30 min at 80°, TLC (Et_2O–petrol, 1:1) afforded 2 mg **4**, IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3650 (OH), 1650, 1590 (PhCO); MS *m/z* (rel. int.): 356.126 (M^+, 100) $C_{20}H_{20}O_6$), 301 (M – C_4H_7, 20), 300 (M – $H_2C{=}C(Me)_2$, 13, RAD), 165 (301 – $C_8H_8O_2$, 50).



1 R = H
2 R = OH



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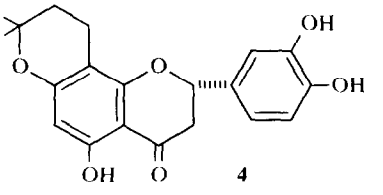

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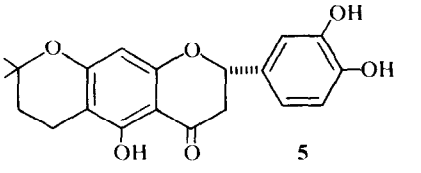

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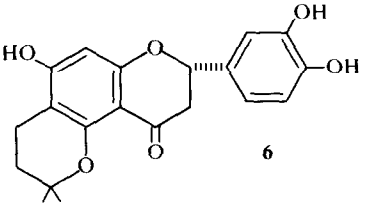

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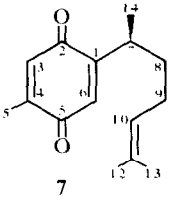

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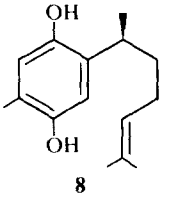

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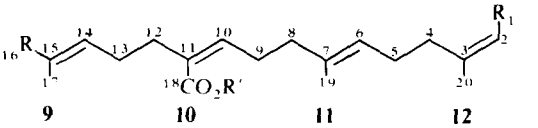
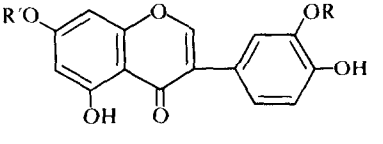


	9	10	11	12
R	CH_2OH	CH_2OH	CHO	CH_2OAc
R′	H	Me	Me	H



13 R = H, R′ = Me
14 R = Me, R′ = H

5,7,3′,4′-Tetrahydroxy-6-[3′,3′-dimethylallyl]-flavanone (**3**). Colourless crystals, mp 188° ($CHCl_3$), IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3540 (OH), 1640 (PhCO); MS *m/z* (rel. int.): 356.126 (M^+, 100) ($C_{20}H_{20}O_6$), 341 (M − Me, 22), 313 (M − C_3H_7, 20), 301 (M − C_4H_7, 24), 165 (301 − $C_8H_8O_2$, 82). 3 mg **3** were cyclized as above. TLC (Et_2O–petrol, 1:1) afforded 1.5 mg **5**, IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3550 (OH), 1650, 1600 (PhCO); MS *m/z* (rel. int.): 356.126 (M^+, 100) ($C_{20}H_{20}O_6$), 301 (22), 165 (95) and 1 mg **6**, IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3450 (OH), 1650 (PhCO); MS *m/z* (rel. int.): 356.126 (M^+, 100) ($C_{20}H_{20}O_6$), 301 (20), 300 (20), 165 (78).

6-Desoxyperezone (**7**). Yellow oil, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3260, 1660, 1610 (quinone); MS *m/z* (rel. int.): 232.146 (M^+, 5) ($C_{15}H_{20}O_2$), 151 (M − C_6H_9, 100). To 10 mg **7** in 1 ml MeOH, 10 mg $NaBH_4$ were added at RT. After 10 min, dil. H_2SO_4 was added. TLC (Et_2O–petrol, 1:3) afforded 9.3 mg **8**, colourless oil, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3605 (OH), 1650 (C=C); MS *m/z* (rel. int.): 234.162 (M^+, 32), ($C_{15}H_{22}O_2$) 151 (100);

$$[\alpha]_{24°}^{\lambda} = \frac{589 \quad 578 \quad 546 \quad 436\,nm}{-33.5 \quad -34.3 \quad -39.8 \quad -76.7} \quad (c = 0.93,\ CHCl_3).$$

Wyethic acid (**9**). Colourless gum, which was purified as its methyl ester **10**, colourless gum, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3610 (OH), 1710, 1635 (C=CCO$_2$R); MS *m/z* (rel. int.): 332.243 (M − H_2O, 1) ($C_{21}H_{32}O_3$), 300 (332 − MeOH, 8), 93 ($C_7H_9^+$, 100). 20 mg **10** in 2 ml CH_2Cl_2 were stirred 1 hr with 30 mg pyridine dichromate. TLC (Et_2O–petrol, 1:1) afforded 15 mg **11**, colourless gum, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 2740, 1680 (C=CCHO), 1720, 1625 (C=CCO$_2$R); MS *m/z* (rel. int.): 328 (M − H_2O, 0.5), 296 (328 − MeOH, 0.5), 81 ($C_6H_9^+$, 100). 10 mg **9** in 0.1 ml Ac_2O were heated 1 hr at 70°. TLC (Et_2O–petrol, 1:1) afforded 8 mg **12**, colourless gum (^1H NMR see Table 3).

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