Phytochemistry, Vol. 23, No. 5, pp. 1135–1137, 1984.
Printed in Great Britain.

0031–9422/84 $3.00 + 0.00

PRENYLATED *p*-COUMARATES FROM *WERNERIA STUEBELII**

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(*Revised received* 31 *August* 1983)

Key Word Index—*Werneria stuebelii*; Compositae; prenylated methyl coumarates.

Abstract—The aerial parts of *Werneria stuebelii* afforded in addition to β-cedrene and bicyclogermacrene eight derivatives of methyl *p*-coumarate, all being formed by prenylation. The structures were elucidated by their molecular formulae and their ^{1}H NMR spectra. The chemotaxonomy of the Andean genus *Werneria* is discussed briefly.

INTRODUCTION

The Andean genus *Werneria* is generally regarded as a member of the tribe Senecioneae [1], but is somewhat anomalous cytologically with high polyploidy [1] and in having Helianthoid rather than Senecioid pollen ultrastructure [2]. Though about 40 species are combined in this genus nothing is known about their chemistry. It therefore was interesting to know whether chemistry would give any further information on the taxonomic position of the genus. We have studied the constituents of *Werneria stuebelii* Hieron and the results are discussed in this paper.

RESULTS AND DISCUSSION

The aerial parts of *Werneria stuebelii*, collected in February 1982 in Peru, afforded bicyclogermacrene and β-cedrene as well as a complex mixture of aromatic compounds. After repeated thin layer chromatography, eight derivatives of methyl *p*-coumarate were isolated, the known 2-prenyl derivative **2** [3], the related methyl ether **3**, the *ortho*-hydroxyketone **4**, the isomeric carbinol **5** and the chromenes **6**–**9**.

The structure of **3**, molecular formula $C_{16}H_{20}O_4$, followed from the ^{1}H NMR spectral data (Table 1). The presence of a methyl *p*-coumarate was indicated by the typical chemical shifts of H-7 and H-8, while the substitution pattern followed from the splitting of the signals of the aromatic protons. Their chemical shifts further indicated that the prenyl side chain was at C-2 as only one aromatic proton signal was at higher field (H-6). The nature of the side chain followed from the coupling $J_{1',2'}$ and the chemical shifts of H-1′ and H-2′ which agreed nicely with those of similar compounds. Compound **3** therefore was methyl 3-[3′,3′-dimethyl-3′-hydroxyallyl]-*p*-coumarate-*O*-methyl ether.

The ^{1}H NMR spectrum of **4** (Table 1) again showed that a derivative of methyl *p*-coumarate was present. The altered side chain and the free phenolic hydroxyl group could be deduced from the low field singlet at δ13.1 and the typical signals of a senecioyl residue (6.81 *qq*, 2.25 *d*, 2.11 *d*). Furthermore the downfield shift of the narrowly split aromatic signal (H-3), as well as that of H-5, strongly supported the substition pattern.

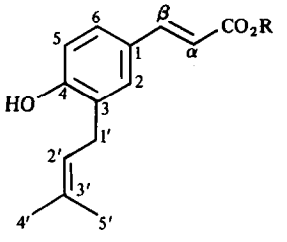
Table 1. ^{1}H NMR spectral data of compounds **3**–**5** (400 MHz, $CDCl_3$, TMS as internal standard)

	3	**4**	**5**
H-2	7.61 *d*	7.90 *d*	7.25 *d*
H-6	7.38 *dd*	7.60 *dd*	7.34 *dd*
H-5	6.86 *d*	7.00 *d*	6.87 *d*
H-β	7.64 *d*	7.60 *d*	7.61 *d*
H-α	6.35 *d*	6.34 *d*	6.27 *d*
H-1′	6.89 *d*	—	4.57 *dd*
H-2′	6.40 *d*	6.81 *qq*	2.97 *dd* 2.85 *dd*
H-4′	1.45 *s*	2.11 *d*	1.83 *br s*
H-5′		2.25 *d*	5.06 *br s* 5.02 *br s*
OMe	3.87, 3.80 *s*	3.72 *s*	3.79 *s*
OH		13.1 *s*	

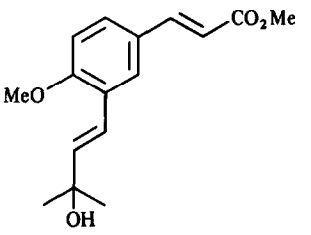
J (Hz): 2, 6 = 2; 5, 6 = 8.5; α, β = 16; compound **3**: 1′, 2′ = 16; compound **4**: 2′, 4′ = 2′, 5′ ~ 1; compound **5**: 1′, $2_1'$ = 8.5; 1′, $2_2'$ = 3.5; $2_1'$, $2_2'$ = 15.

The ^{1}H NMR spectral data of **5**, molecular formula $C_{15}H_{18}O_4$, indicated again the presence of a monosubstituted methyl *p*-coumarate. The nature of the substituent followed from the corresponding ^{1}H NMR signals. A pair of doublets at δ2.97 and 2.85 and a double doublet at 4.57 as well as the typical signals of an isopropenyl group (1.83 *br s*, 5.06 *br s* and 5.02 *br s*) nicely agreed with the proposed side chain. A hydrogen bridge between the phenolic and the benzylic hydroxyl groups was present. Accordingly, a clear differentiation of the coupling $J_{1',2'}$ could be observed.

The ^{1}H NMR spectral data of the isomeric chromenes **6** and **7** (Table 2) as well as the molecular formulae ($C_{15}H_{16}O_3$) agreed with the proposed structures. The presence of *cis*, *trans*-isomeric *p*-coumarates followed from the couplings of H-9 and from the typical chemical shifts of H-5, H-9 and H-10. The splitting pattern and the



R
1 H
2 Me



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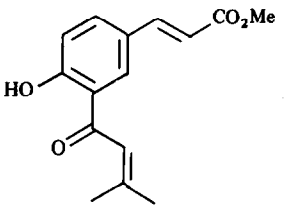

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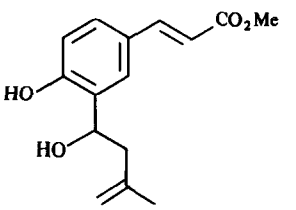

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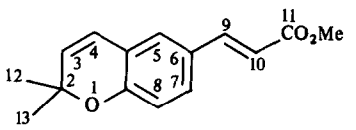
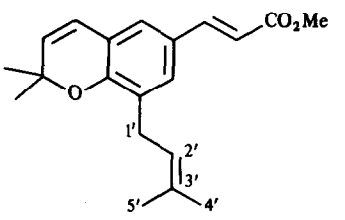


6 9,10 *E*
7 9,10 *Z*



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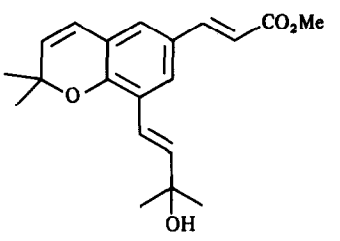

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chemical shifts of the aromatic protons and the typical signals of a 2,2-dimethylchromene led to the structures of these isomers.

The ^{1}H NMR spectrum (Table 2) and also the molecular formula ($C_{20}H_{24}O_3$) showed that **8** differed from **6** only by an additional 3',3'-dimethylallyl substituent. Accordingly, only two aromatic signals with a *meta* coupling were observed and the typical signals of the side chain (3.19 *br d*, 5.19 *tqq*, 1.67 *d* and 1.66 *d*) clearly established its nature.

The molecular formula of **9** ($C_{20}H_{24}O_4$) showed that this ester differed from **8** by an additional oxygen. The ^{1}H NMR spectrum (Table 2) showed that a derivative of **6** was present with a 3'-hydroxy-3',3'-dimethylallyl side chain at C-8. The position of this substituent followed from the couplings of the aromatic protons. The chromene **6** we have named werneria chromene.

While prenylated *p*-hydroxyacetophenone derivatives are widespread in the Compositae, prenylated coumarates so far are rare though cinnamates and coumarates are common. Compound **2** was reported from a *Baccharis* species [3], the corresponding acid **1** and the 2,6-*bis*-[3,3-dimethylallyl]-coumaric acid was isolated from a *Flourensia* species [4]. The latter also was reported from an other *Baccharis* species [5]. An *O*-prenylated *p*-coumaric acid was isolated from a *Hemizonia* species [6] and from a *Conyza* species [7]. Since these genera are placed in two different tribes, the chemotaxonomic relevance of these compounds is still in question. Compounds characteristic of most members of the tribe Senecioneae, such as furoeremophilanes, have not been found in this study of *Werneria stuebelii*.

Table 2. ^{1}H NMR spectral data of compounds **6–9** (400 MHz, $CDCl_3$, TMS as internal standard)

	6	7	8	9
H-3	5.62 *d*	5.61 *d*	5.57 *d*	5.68 *d*
H-4	6.28 *d*	6.31 *d*	6.24 *d*	6.30 *d*
H-5	7.12 *d*	7.47 *d*	7.09 *d*	7.05 *d*
H-7	7.26 *dd*	7.49 *dd*	6.94 *d*	7.45 *d*
H-8	6.74 *d*	6.73 *d*	—	—
H-9	7.58 *d*	6.78 *d*	7.52 *d*	7.60 *d*
H-10	6.26 *d*	5.80 *d*	6.19 *d*	6.40 *d*
H-12, 13	1.42 *s*	1.43 *s*	1.36 *s*	1.40 *s*
H-1′	—	—	3.19 *br d*	6.84 *d*
H-2′	—	—	5.19 *tqq*	6.29 *d*
H-4′	—	—	1.67 *d*	1.38 *s*
H-5′	—	—	1.66 *d*	
OMe	3.76 *s*	3.72 *s*	3.71 *s*	3.79 *s*

J (Hz) 3,4 = 10; 5,7 = 2; 7,8 = 8.5; 9,10 = 16 (compound **7**: 9, 10 = 13); compound **8**: 1′, 2′ = 7.5; 2′, 4′ = 2′, 5′ = 1; compound **9**: 1′, 2′ = 16.5.

EXPERIMENTAL

The air dried plant material (200 g) (voucher RMK 9062) was extracted with Et_2O–petrol, 1:2, and the resulting extract was separated first by CC (SiO_2, 100 g) (50 ml fractions, 1–3 petrol, 4–6 Et_2O–petrol, 1:10, 7–9 Et_2O–petrol, 1:3, 10–12 Et_2O–petrol, 1:1, 13–15 Et_2O, 16–18 Et_2O–MeOH, 20:1). Fractions 1–3 afforded on TLC (SiO_2 coated with $AgNO_3$ coated, detection by spraying with $KMnO_4$-solution) 3 mg bicyclogermacrene and 20 mg *β*-cedrene (identified by comparing all spectral data with those of authentic material). Fractions 4–6 gave by TLC (SiO_2 PF 254, detection by UV 255 nm Et_2O–petrol, 1:10, several developments) 5 mg **7**, (R_f 0.35) followed by 15 mg **8** (R_f 0.33) and 200 mg **6** (R_f 0.30). Fractions 7–12 gave by TLC (SiO_2, Et_2O–petrol, 1:3, two developments) 80 mg **2** (R_f 0.55) (400 MHz ^{1}H NMR spectrum identical with that of authentic material) and 50 mg **4** (R_f 0.45). Fractions 13–18 afforded by TLC (SiO_2, Et_2O–petrol, 3:1) 50 mg **3** (R_f 0.45) and a mixture of **5** and **9** (R_f 0.5) which gave by repeated TLC (SiO_2, Et_2O–petrol, 1:1, five developments 3 mg **9** (R_f 0.35) and 5 mg **5** (R_f 0.35).

The purity of compounds which could not be induced to crystallize were tested by TLC in different solvent mixtures and by 400 MHz ^{1}H NMR spectroscopy.

Methyl-3-[3′,3′-*dimethyl*-3′-*hydroxyallyl*]-p-*coumarate*-O-*methyl ether* (**3**). Colourless gum (free of impurities by TLC, ^{1}H NMR); IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3600 (OH), 1720, 1640 (C=CCO_2R), 1600, 985 (*trans* CH=CH); MS *m/z* (rel. int.): 276.136 [M]$^+$ (32) ($C_{16}H_{20}O_4$), 261 [M − Me]$^+$ (9), 258 [M − H_2O]$^+$ (7), 245 [M − OMe]$^+$ (11), 233 [261 − CO]$^+$ (6), 229 [261 − MeOH]$^+$ (24), 211 [229 − H_2O]$^+$ (23), 205 [233 − CO]$^+$ (81), 201 [229 − CO]$^+$ (20), 187 [205 − H_2O]$^+$ (100), 173 [201 − CO]$^+$ (11).

Methyl-3-*senecioyl*-p-*coumarate* (**4**). Yellow crystals, mp 114° (Et_2O–petrol), IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3500–2600, 1640 (*O*-hydroxy ketone), 1715 (C=CCO_2R), 990 (*trans* CH=CH); MS *m/z* (rel. int.): 260.105 [M]$^+$ (11) ($C_{15}H_{16}O_4$), 245 [M − Me]$^+$ (100), 229 [M − OMe]$^+$ (7), 213 [245 − MeOH]$^+$ (30), 205 [M − C_4H_7]$^+$ (22), 173 [205 − MeOH]$^+$ (17), 145 [173 − CO]$^+$ (10).

Methyl-3-[3′-*methyl*-1′-*hydroxy*-*but*-3′-*en*-1′-*yl*]-p-*coumarate* (**5**). Colourless gum (free of impurities by TLC, ^{1}H NMR); IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3590, 3380 (OH), 1720, 1630, 980 (C=CCO_2R); MS *m/z* (rel. int.): 262.121 [M]$^+$ (18) ($C_{15}H_{18}O_4$), 244 [M − H_2O]$^+$ (17), 229 [244 − Me]$^+$ (58), 70 (100), 69 (88); CI (isobutane): 263 [M + 1]$^+$ (15), 245 [263 − H_2O]$^+$ (28), 71 (100).

Werneria chromene (**6**). Colourless crystals, mp 64° (petrol); IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1720, 1635 (C=CCO_2R), 1610 (C=C); MS *m/z* (rel. int.): 244.110 [M]$^+$ (18) ($C_{15}H_{16}O_3$), 229 [M − Me]$^+$ (100), 213 [M − OMe]$^+$ (4), 197 [229 − MeOH]$^+$ (1), 169 [197 − CO]$^+$ (6).

9-*Z*-*Werneria chromene* (**7**). Colourless gum (free of impurities by TLC, ^{1}H NMR); IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1725, 1630, (C=CCO_2R), 1595 (C=C); MS *m/z* (rel. int.): 244.110 [M]$^+$ (15), 229 [M − Me]$^+$ (100), 213 [M − OMe]$^+$ (3), 197 [229 − MeOH]$^+$ (1), 169 [197 − CO]$^+$ (6).

8-[3′,3′-*Dimethylallyl*]-*werneria chromene* (**8**). Colourless gum (checked for impurities as before); IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1725, 1635 (C=CCO_2R), 1595 (C=C); MS *m/z* (rel. int.): 312.173 [M]$^+$ (21) ($C_{20}H_{24}O_3$), 297 [M − Me]$^+$ (100), 281 [M − OMe]$^+$ (3), 244 [M − isoprene]$^+$ (11), 229 [244 − Me]$^+$ (75), 213 [244 − OMe]$^+$ (3).

8-[3′,3′-*Dimethyl*-3′-*hydroxyallyl*]-*werneria chromene* (**9**). Colourless gum (checked for impurities as before); IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3600 (OH), 1720, 1640 (C=CCO_2R), 1605, 985 (*trans* CH=CH); MS *m/z* (rel. int.): 328.167 [M]$^+$ (29), 313 [M − Me]$^+$ (100), 295 [313 − H_2O]$^+$ (10).

Acknowledgements—We thank the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie for financial support.

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