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SESQUITERPENE LACTONES, GERANYLNEROL AND TREMETONE DERIVATIVES FROM *AGERATINA* SPECIES

FERDINAND BOHLMANN, SHANTA BANERJEE, CHRISTIAN WOLFRUM, JASMIN JAKUPOVIC, ROBERT M. KING* and HAROLD ROBINSON*

Institute for Organic Chemistry, Technical University of Berlin, D-1000 Berlin 12, West Germany; *Smithsonian Institution, Department of Botany, Washington, DC 20560, U.S.A.

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Key Word Index—*Ageratina tristis*; *A. azangaroensis*; Compositae; sesquiterpene lactones; germacranolide; heliangolide; guaianolide; 19-acetoxy-20-hydroxygeranylnerol; tremetone derivative.

Abstract—The investigation of two further *Ageratina* species afforded, in addition to known compounds, some new ones, a germacrolide, a heliangolide, a guaianolide, a geranylnerol derivative and a tremetone derivative.

INTRODUCTION

So far the chemical investigation of species of the large genus *Ageratina* (Compositae, tribe Eupatorieae, subtribe Ageratinae) has shown that *p*-hydroxyacetophenone [1–6] and thymol derivatives [3, 4, 6–8] are widespread. Sesquiterpene lactones were reported only from three species [7, 9, 10]. We have now studied the constituents from *A. azangaroensis* (Sch. Bip. et Wedd.) K. et R. The aerial parts gave 5-methoxytremetone, 10-angeloyloxy-8,9-epoxythymol isobutyrate, 4-hydroxyacetophenone and its 3,5-*bis*-dimethylallyl derivative [5] as well as the tremetone derivative **1**.

RESULTS AND DISCUSSION

The structure of **1** followed directly from the molecular formula and the ^{1}H NMR spectrum (see Experimental).

The aerial parts of *A. tristis* (DC.) K. et R. gave several widespread compounds (see Experimental), thymol derivatives (see Experimental), the geranylnerol derivative **2**, the heliangolides **4** [11] and **5** [12] as well as **6**, the costunolide derivative **7** and the guaianolide **8**. The structure of **2** followed from the ^{1}H NMR spectral data (Table 1) and from those of the corresponding dialdehyde **3** obtained from **2** by manganese dioxide oxidation. Careful spin decoupling allowed the assignment of all signals although a few were overlapped multiplets (H-8, H-9 and H-12, H-13). However, as the sequences H-1, H-2, H-4, H-5 and H-19 could clearly be established, the relative positions of the oxygen functions could be determined. From the chemical shift of H-1 in the spectrum of **3** the configuration of the Δ^2-double bond could be deduced. Comparison of the chemical shifts of the remaining signals with those of similar compounds indicated the configurations of the Δ^6- and Δ^{10}-double bonds.

The structure of **6** could be deduced from the ^{1}H NMR spectrum (Table 2), which was close to that of provincialin, an isomer of **6**, differing only in the position of one of the hydroxyl groups of the ester residue [11].

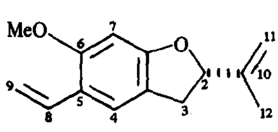
The ^{1}H NMR spectrum of **7** (Table 2) was close to that of the corresponding tiglate [13]. As the couplings were identical, the stereochemistry was also the same. The structure of **8** could also be deduced from the ^{1}H NMR spectrum (Table 2), which was close to that of kauniolide [14] and its 8β-acyloxy derivative [15]. The nature of the ester residue followed from the characteristic signals.

The chemistry of the two *Ageratina* species differed remarkably. While *A. azangaroensis* is placed in the subgenus *Ageratina*, *A. tristis* belongs to *Neogreenella* [16]. Two other *Ageratina* species from which lactones have so far been isolated [9, 12] are members of the latter subgenus. This conforms with the known distribution of lactone-bearing glandular punctations in the genus, being absent in subgenus *Ageratina* and present in *Neogreenella*.

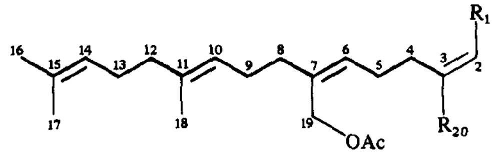
Table 1. ^{1}H NMR spectral data of **2** and **3** (400 MHz, $CDCl_3$, TMS as internal standard)

	2	**3**
H-1	4.18 *br d*	10.26 *d*
H-2	5.69 *br t*	6.53 *d*
H-4	2.21 *br t*	2.76 *br t*
H-5	2.16 *m*	2.33 *dt*
H-6	5.40 *br t*	5.36 *br t*
H-8	2.05 *m*	2.07 *m*
H-9	1.96 *m*	1.98 *m*
H-10	5.08 *br t*	5.08 *br t*
H-12	2.05 *m*	2.07 *m*
H-13	1.96 *m*	1.96 *m*
H-14	5.08 *br t*	5.08 *br t*
H-16	1.66 *br s*	1.68 *br s*
H-17	1.57 *br s*	1.60 *br s*
H-18		1.59 *br s*
H-19	4.57 *br s*	4.52 *br s*
H-20	4.07 *br s*	9.66 *s*
OAc	2.05 *s*	2.07 *s*

J (Hz): 1, 2 = 4, 5 = 5, 6 = 9, 10 = 13, 14 = 7.

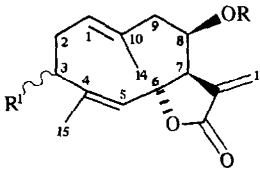


1

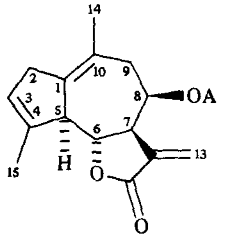


2 R = CH_2OH

3 R = CHO

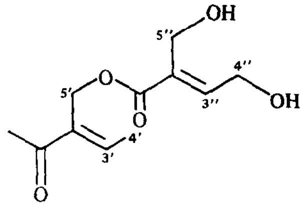


	4	5	6	7
R	H	H	A	H
R^1	αOAc	βOAc	βOAc	βOAc (4E)



8

A =



EXPERIMENTAL

The air-dried aerial parts of *Ageratina tristis* (300 g, voucher 14/84, deposited at the U.S. National Herbarium, Washington, U.S.A.; collected in January 1984 near Kingston, Jamaica) were extracted with Et_2O–MeOH–petrol (1:1:1) and worked up in the usual fashion [17]. CC (SiO_2) fractions were as follows: 1 (petrol), 2 (Et_2O–petrol, 1:9), 3 (Et_2O–petrol, 1:1) and 4 (Et_2O and Et_2O–MeOH, 9:1). TLC (SiO_2, PF 254) of fraction 1 (petrol) gave 12 mg germacrene D and 10 mg α-humulene. TLC of fraction 2 (Et_2O–petrol, 1:9) afforded 80 mg taraxasteryl acetate, 40 mg lupeyl acetate, 10 mg 10-isovaleryloxy-8,9-epoxythymol, 5 mg of the 2-methylbutyryloxy-, 15 mg of the isobutyryloxy- and 45 mg of acetoxy derivative, as well as 55 mg of 5-methoxy-10-acetoxy-8,9-epoxythymol. TLC of fraction 3 (Et_2O–petrol, 3:1) gave 50 mg sakuranetin and 15 mg 7-*O*-methyl aromadendrin. TLC of fraction 4 (Et_2O–petrol, 2:1, several developments) gave four bands (4/1–4/4). TLC of 4/1 (Et_2O–petrol, 7:3, 3 developments) gave 8 mg **2** (R_f 0.20). TLC of 4/2 gave 5 mg **4**, 1 mg **5** and 1.5 mg **7** (R_f 0.58). TLC of 4/3 (Et_2O–petrol, 4:1, 2 developments and then Et_2O) gave 20 mg **8** (R_f 0.43) and HPLC (RP 8, MeOH–H_2O, 3:2, *ca* 100 bar, flow rate 3 ml/min) afforded 15 mg **6** (R_t 5.3 min). All compounds were homogeneous by 400 MHz, ^1H NMR and by TLC.

The aerial parts of *Ageratina azangaroensis* (365 g, voucher RMK 9037, deposited at the U.S. National Herbarium, Washington, U.S.A.; collected in January 1982 in Peru) were worked up in the usual fashion [17]. CC fractions were as follows: 1 (Et_2O–petrol, 1:9 and Et_2O–petrol, 1:3) and 2 (Et_2O–petrol, 1:1 and Et_2O–MeOH, 9:1). TLC of fraction 1 (Et_2O–petrol, 1:9) gave 4 mg **9** (R_f 0.45). TLC of fraction 2 (Et_2O–petrol, 1:1) gave 7 mg 10-angeloyloxy-8,9-epoxythymol isobutyrate and 20 mg bis-[3,3-dimethylallyl]-*p*-hydroxyacetophenone, 3 mg 5-methoxytremetone and 7 mg *p*-hydroxyacetophenone.

Known compounds were identified by comparing the 400 MHz, ^1H NMR spectra with those of authentic material and by co-TLC.

6-Methoxy-5-vinyl-desacetyl tremetone (**1**). Colourless oil; MS *m/z* (rel. int.): 216.115 $[M]^+$ (65) (calc. for $C_{14}H_{16}O_2$: 216.115), 201 $[M-Me]^+$ (100); ^1H NMR ($CDCl_3$): δ5.19 *br dd* (H-2), 2.98 *dd* (H-3), 3.29 *dd* (H-3′), 7.27 *s* (H-4), 6.40 *s* (H-7), 6.99 (H-8), 5.56 *dd* (H-9), 5.09 *dd* (H-9′), 4.90 *br s* (H-11), 5.07 *br s* (H-11′), 1.77 *br s* (H-12), 3.81 *s* (OMe) [*J* (Hz): 2,3 = 8; 2,3′ = 9; 3,3′ = 15; 8,9 = 17; 8,9′ = 10; 9,9′ = 1.5].

19-Acetoxy-20-hydroxygeranylnerol (**2**). Colourless oil; IR $\nu_{\max}^{CCl_4}$ cm^{-1}: 3600 (OH), 1750 (OAc); MS *m/z* (rel. int.): 364.261 $[M]^+$ (0.2) (calc. for $C_{22}H_{36}O_4$: 364.261), 304 $[M-HOAc]^+$ (2), 286 $[304-H_2O]^+$ (1.5), 69 $[C_5H_9]^+$ (100). 6 mg **2** in 5 ml Et_2O

Table 2. ^{1}H NMR spectral data of **6**–**8** (400 MHz, $CDCl_3$, TMS as internal standard)

	6	**7**	**8**
H-1	5.19 *br d*	4.88 *br dd*	—
H-2	2.70 *m*	2.55 *m*	3.05 *br d*
H-2′	2.28 *m*	2.36 *ddd*	2.94 *br d*
H-3	5.28 *br s*	5.22 *dd*	5.54 *br s*
H-5	5.17 *dq*	4.90 *br d*	3.38 *br d*
H-6	5.89 *br d*	5.22 *dd*	4.09 *dd*
H-7	2.98 *br s*	2.78 *br ddd*	3.05 *m*
H-8	5.24 *t*	4.60 *br dd*	5.64 *br d*
H-9	2.73 *br d*	2.72 *br dd*	2.55 *m*
H-9′	2.46 *br d*	2.29 *dd*	
H-13	6.24 *d*	6.42 *d*	6.10 *d*
H-13′	5.76 *d*	5.59 *d*	5.43 *d*
H-14	1.75 *br s*	1.65 *br s*	1.60 *br s*
H-15	1.80 *br s*	1.74 *d*	1.92 *br s*
OAc	2.09 *s*	2.11 *s*	—
H-3′	6.95 *q*	—	6.84 *q*
H-4′	1.88 *d*	—	1.86 *d*
H-5′	4.98 *d* 4.86 *d*	— —	4.94 *d* 4.82 *d*
H-3″	7.00 *br t*	—	6.98 *t*
H-4″	4.43 *dd* 4.30 *dd*	—	4.43 *dd*
H-5″	4.18 *br s*	—	4.24 *br s*

J (Hz): 3′,4′ = 7; 5′,5′ = 12; 3″,4″ = 6; 4″,4″ = 15; compound **6**: 1,2 ~ 10; 5,6 = 11; 5,15 = 1.5; 6,7 ~ 1.5; 7,8 ~ 2.5; 7,13 = 2.3; 7,13′ = 1.8; 9,9′ = 14; compound **7**: 1,2 = 11.5; 1,2′ = 4; 2,2′ = 15; 2′,3 = 10; 2,3 = 4; 5,6 = 11; 6,7 = 9; 7,8 = 7,13 = 3.5; 7,13′ = 3; compound **8**: 2,2′ = 20; 5,6 = 6,7 = 10; 7,8 ~ 2; 7,13 = 3.3; 7,13′ = 3.

was stirred for 2 hr with 100 mg MnO_2. TLC (Et_2O–petrol, 3:1) gave 4 mg **3**, colourless oil; ^{1}H NMR: see Table 1.

4′-Desoxy-4″-hydroxyprovincialin (**6**). Colourless oil; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3600 (OH), 1775 (γ-lactone), 1750 (OAc), 1720 (C=CCO$_2$R); MS *m/z* (rel. int.): 518.115 $[M]^+$ (6) (calc. for $C_{27}H_{34}O_{10}$: 518.115), 458 $[M-HOAc]^+$ (1), 289 $[M-OCOR]^+$ (19), 288 $[M-RCO_2H]^+$ (2), 246 $[288-\text{ketene}]^+$ (22), 229 $[RCO]^+$ (44), 228 $[288-HOAc]^+$ (66), 213 $[228-Me]^+$ (17), 211 $[229-H_2O]^+$ (12), 183 $[211-CO]^+$ (16), 99 $[C_4H_6(OH)CO]^+$ (100), 81 $[99-H_2O]^+$ (50), 69 $[99-CH_2O]^+$ (54).

3β-Acetoxy-8β-hydroxycostunolide (**7**). Colourless oil; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3600 (OH), 1775 (γ-lactone), 1750 (OAc); MS *m/z* (rel. int.): 306.147 $[M]^+$ (2) (calc. for $C_{17}H_{22}O_5$: 306.147), 246 $[M-HOAc]^+$ (8), 57 (100).

8β-[5′-[4,5-Dihydroxytigloyloxy]-tigloyloxy]-kauniolide (**8**). Colourless oil; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3600 (OH), 1775 (γ-lactone), 1720 (C=CCO$_2$R); MS *m/z* (rel. int.): 228.115 $[M-RCO_2H]^+$ (40) (calc. for $C_{15}H_{18}O_2$: 228.115), 199 $[C_4H_6(OH)CO]^+$ (100).

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