Phytochemistry, Vol. 27, No. 7, pp. 2251–2254, 1988.
Printed in Great Britain.

0031-9422/88 $3.00 + 0.00

NERYLGERANIOL DERIVATIVES AND TWO CLERODANES FROM *VITTADINIA GRACILIS*

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(*Received* 18 *September* 1987)

Key Word Index—*Vittadinia gracilis*; *V. cuneata*; Compositae; diterpenes; nerylgeraniol derivatives; clerodanes.

Abstract—The aerial parts of *Vittadinia gracilis* afforded in addition to spathulenol four nerylgeraniol derivatives and two clerodane dilactones. The structures were elucidated by high field NMR spectroscopy and a few chemical transformations. The chemotaxonomic situation is discussed briefly.

INTRODUCTION

The distinctive genus *Vittadinia* (Compositae, tribe Astereae, subtribe Asterinae) with 27 Australian species and one each in New Caledonia and New Zealand [1] has not been studied very much chemically. So far only the absence of acetylenes [2] and the isolation of triterpenes and steroids from one species [3] are reported. As the delimitation of subtribes is still a problem [4] further chemical studies may be useful in this tribe. We now have studied two species, *V. gracilis* (Hook. f.) N. Burb. and *V. cuneata DC. f. cuneata*. The results are discussed in this paper.

RESULTS AND DISCUSSION

The extract of aerial parts of *V. gracilis* afforded spathulenol, the nerylgeraniol derivatives **1**–**4** and the clerodanes **5** and **6**. The ^{1}H NMR spectra of **1** and **2** (Table 1) clearly indicated the presence of nerylgeraniol derivatives. In the spectrum of **1** three olefinic methyls and two hydroxymethyl broadened singlets and one hydroxymethyl doublet were visible. Accordingly, a nerylgeraniol derivative, where two methyl groups were hydroxylated, was present. The highest ion in the mass spectrum led to the molecular formula $C_{20}H_{30}O$. However, after acetylation a triacetate was obtained which gave the expected molecular ion required for $C_{26}H_{40}O_6$. The second compound obviously was the corresponding aldehyde which by boranate reduction could be transformed to a triol identical with the natural diterpene. The remaining structural problems, the position of the hydroxy groups and the configuration of the double bonds could be solved using the aldehyde **2** as in its ^{1}H NMR spectrum the signals were much better separated allowing clear spin decouplings. The obtained sequences required an aldehyde group at C-11. Irradiation at δ5.08 sharpened two methyl signals and collapsed a broadened quartet at δ2.03 to a triplet. Accordingly, these signals were due to H-14 and H-13. Irradiation of H-13 collapsed the triplet at δ2.20 to a singlet (H-12). Irradiation of the latter sharpened the signal of the proton in the β-position to the aldehyde moiety thus fixing the position of this group. The chemical shift of the aldehyde proton required an *E*-configuration of the 10.11-double bond. Further decouplings clearly showed that a hydroxy group was at C-19. Clear NOE's between H-1 and H-20 supported this assumption and also established the configuration of the 2.3-double bond. Similarly the *Z*-configuration of the 6.7-double bond was determined.

The aldehydes **3** and **4** partly could be separated by repeated HPLC. The ^{1}H NMR spectra (Table 1) indicated that we were dealing most likely with epimeric compounds. Comparison of the spectra with that of **2** indicated that non-conjugated aldehydes were present. This was further supported by the absence of the fourth olefinic proton signal which was replaced by low field signals at δ3.66 and 3.71, respectively. These data showed that tetrahydropyrane derivatives might be present. Careful spin decoupling led to sequences which agreed well with this proposal. The obtained sequences required the aldehyde group to be at C-11 with an ether ring between C-10 and C-19. Again the configuration of the double bonds followed from the NOE's between H-1 and H-20 as well as between H-5 and H-19. As the signals of H-10, H-11 and H-18 differed most in the spectra of **3** and **4** it was very likely that the aldehydes were epimeric at C-11. Boranate reduction of the epimers afforded the diols **3a** and **4a**. Inspection of their ^{1}H NMR spectra, and of models, indicated that in both diols a hydrogen bridge between the hydroxy group at C-18 and the ether oxygen was very likely. This allowed the elucidation of the relative configurations by NOE. A clear effect between H-10, H-8 axial and H-19 in the case of **4a** required an axial position of H-10. As the latter gave no NOE with H-18 while H-9 equatorial gave an effect with H-12 the configuration at C-11 was settled (see formulae **4b**). The epimers showed no optical rotations and therefore they could be artifacts. However, treatment of **3** with *tert*-butylate at room temperature only led to condensations. Compounds **3** and **4** we have named vittadinal and *epi*-vittadinal, respectively.

The diterpene **5** had molecular formula $C_{20}H_{20}O_6$ indicating a high degree of unsaturation. In the ^{1}H NMR spectrum (Table 2) all signals could be assigned by spin

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

H	1	2	3	4	1Ac	3a	C_6D_6	4a
1	4.11 *br d*	4.12 *br d*	4.14 *br d*	4.13 *br d*	4.57 *br d*	4.16	4.12 *dd*	4.16 *dd*
						4.10	4.05 *dd*	4.12 *dd*
2	5.35 *br t*	5.36 *br t*	5.41 *br t*	5.41 *br t*	5.33 *br t*	5.40	5.42 *br t*	5.41 *br t*
4	2.05 *m*	2.04 *m*	2.07 *m*	2.05 *m*	2.05 *m*	*	*	*
5	2.15 *m*	2.25 *m*	2.05 *m*	2.12 *m*	2.20 *m*	*	*	*
6	5.41 *br t*	5.27 *br t*	5.29 *br t*	5.28 *br t*	5.39 *br t*	5.17	5.10 *br t*	5.18 *br t*
8	2.05 *br t*	2.31 *br t*	2.31 *br t*	2.27 *m*	2.05 *m*	*	*	*
9	2.20 *br q*	2.51 *br q*	1.80 *m*	1.70 *m*	2.20 *m*	*	*	*
9′			1.50 *m*	1.47 *dddd*				
10	5.27 *t*	6.45 *t*	3.66 *ddd*	3.71 *ddd*	5.39 *br t*	3.65	3.50 *ddd*	3.46 *ddd*
11	—	—	2.31 *m*	2.44 *dddd*	—	1.83	1.79 *dddd*	1.59 *m*
12	2.19 *br s*	2.04 *br t*	1.77 *m*	1.81 *dddd*	2.20 *m*	*	*	1.40 *t*
12′			1.50 *dddd*	1.58 *dddd*				
13		2.03 *br q*	2.00 *m*	2.05 *m*		*	*	*
13′				1.96 *ddt*				
14	5.10 *br t*	5.08 *br t*	5.07 *br t*	5.07 *br t*	5.10 *br t*	5.08	5.23 *br t*	5.09 *br t*
16	1.67 *br s*	1.67 *br s*	1.68 *br s*	1.67 *br s*	1.68 *br s*	1.67	1.71 *br s*	1.67 *br s*
17	1.59 *br s*	1.56 *br s*	1.59 *br s*	1.57 *br s*	1.59 *br s*	1.60	1.61 *br s*	1.59 *br s*
18	4.07 *s*	9.34 *s*	9.69 *s*	9.72 *s*	4.58 *s*	3.71	3.76 *dd*	3.81 *dd*
18′						3.62	3.69 *dd*	3.60 *dd*
19	4.01 *br s*	4.11 *br s*	4.55 *br d*	4.57 *dd*	4.48 *br s*	4.57	4.51 *dd*	4.58 *br d*
19′			3.73 *br d*	3.75 *br d*		3.73	3.58 *br d*	3.72 *br d*
20	1.67 *br s*	1.68 *br s*	1.67 *br s*	1.67 *br s*	1.69 *br s*	1.68	1.49 *br s*	1.68 *br s*

* Overlapped multiplets.

J[Hz]: 1,2 = 4,5 = 5,6 = 8,9 = 9,10 = 12,13 = 13,14 ~ 7; compounds **3** and **4**: 6,19 ~ 1.5; 8,9 = 9,10 = 10,11 ~ 5; 9,9′ = 12; 9′,10 = 2; 11,12 ~ 6; 11,12′ ~ 3; 11,18 = 2.5; 12,12′ = 14; 19,19′ = 13; compound **3a**: 9,10 = 11; 9′,10 = 2; 10,11 = 4; 11,18 = 7; 11,18′ = 3.5; 18,18′ = 11; 19,19′ = 12; compound **4a**: 9,10 = 11; 9′,10 = 2; 10,11 = 6; 11,18 = 2.5; 11,18′ = 6; 18,18′ = 11; 19,19′ = 12.

decoupling. The presence of a β-substituted furan was obvious. Furthermore, many signals were close to those of bacchotricuneatin C [5]. However, a singlet at δ 5.56 and the absence of a pair of doublets (H-20) required a somewhat changed situation. The ^{13}C NMR spectrum (see Experimental) required the presence of a dilactone and a doublet at δ 107.3 agreed with the presence of an acetal carbon. Accordingly, an oxidation product of bacchotricuneatin C could be excluded as the acetal proton was a singlet at δ 5.56. The resulting structure, therefore, was **5** which we have named vittagraciliolide. The ^{13}C NMR data were in part very close to those of bacchotricuneatin A [5]. The stereochemistry at all five chiral centres followed from the observed NOE's. Thus, clear effects were obtained between H-20, H-19 and H-19′, between H-8, H-10 and H-11′, between H-12, H-11 and H-1e as well as between H-10, H-8, H-11 and H-6β. Inspection of a model showed that these results, especially strong NOE's of H-20 required the specified stereochemistry.

The ^{1}H NMR spectrum of **6** (Table 2) was close to that of bacchotricuneatin A [5]. A threefold doublet δ4.57 indicated the presence of a hydroxy derivative and the coupling of the corresponding proton with the olefinic signal (δ6.74 *d*) established the position while the coupling required a β-configuration of the hydroxyl group if compared with the ^{1}H NMR data of a corresponding monolactone [6]. The presence of a 12-epimer followed from the changed ^{1}H NMR signal.

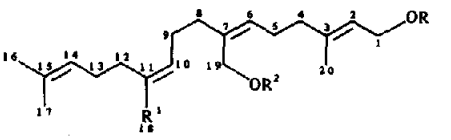
The aerial parts of *V. cuneata* only gave the bisabolol derivative **7**. The ^{1}H NMR spectrum (see Experimental) was close to that of an 1-hydroxy-bisabol-2-ene [7]. However, the isopropylidene signals were replaced by those of a hydroxyisopropyl group. Accordingly, 1,12-dihydroxybisabol-2-ene (**7**) was present. The relative configuration at C-1 and C-7 followed from the observed couplings of H-1 as both epimers of 1-hydroxybisabolene are known [5]. However, the absolute configuration and the relative stereochemistry at C-10 could not be determined.

The isolation of the furoclerodane dilactones from *Vittadinia* may be of chemotaxonomic importance. Similar diterpenes are present in *Aster alpinus* [8], *Conyza* species [9] and especially in *Baccharis* species [5, 10–13]. Furoclerodanes are widespread in the whole tribe and have been reported from *Baccharis*, *Conyza*, *Felicia*, *Grangea*, *Guttierezia*, *Heteropappus*, *Hinterhubera*, *Nidorella*, *Olearia* and *Solidago*. Perhaps the combination of the rare nerylgeraniol derivatives and of furoclerodane dilactones may be characteristic. Investigation of further

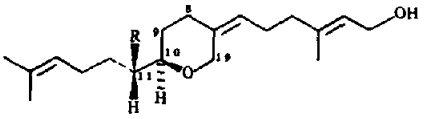
Table 2. ^{1}H NMR spectral data of **5** and **6** (400 MHz, $CDCl_3$, δ-values)

H	5	6
1α	1.40 *dddd*	1.36 *br t*
1β	1.91 *br d*	1.85 *m*
2α	2.53 *dddd*	4.57 *ddd*
2β	2.31 *dddd*	
3	6.83 *dd*	6.74 *d*
6α	2.11 *ddd*	2.15 *ddd*
6β	1.44 *ddd*	1.36 *br t*
7α	1.87 *dddd*	1.80 *m*
7β	2.27 *m*	2.23 *m*
8	2.76 *dd*	2.41 *dd*
10	2.18 *dd*	2.33 *br d*
11α	2.62 *dd*	2.28 *dd*
11β	2.07 *dd*	1.87 *dd*
12	5.35 *t*	5.56 *dd*
14	6.39 *br s*	6.43 *br s*
15	7.39 *t*	7.43 *t*
16	7.41 *br s*	7.47 *br s*
19α	4.00 *dd*	3.97 *dd*
19β	4.34 *d*	4.34 *d*
20	5.56 *s*	0.93 *s*

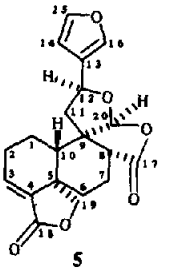
J[Hz]: Compound **5**: 1α,1β = 1α,10 = 12.5; 1α, 2α = 4; 1α,2β = 12; 1β,2α = 1.5; 1β,2β = 4; 1β,10 = 1.5; 2α,2β = 18; 2α,3 = 7.5; 2β,3 = 2; 6α,6β = 14; 6α,7α = 4.5; 6α,7β = 3; 6β,7α = 11; 6β,7β = 5; 6β,19α = 1.5; 7α,7β = 12; 7α,8 = 10.5; 7β,8 = 8; 11α,11β = 14; 11α,12 = 11β,12 = 8; 14,15 = 15,16 = 1.5; compound **6**: 1α,1β = 1α,10 = 12; 1α,2 = 3; 1β,2 = 2; 2,3 = 6.5; 6α,6β = 13; 6α,7α = 6α,7β = 3; 6β,7α = 12; 7α,8 = 12; 7β,8 = 4; 11α,11β = 13; 11α,12 = 5; 11β,12 = 10; 14,15 = 15,16 = 1.5.



1 **1Ac** **2**
R¹ CH_2OH CH_2OAc CHO
R² H Ac H



3 **3a** **4** **4a**
11αH 11αH 11βH 11βH
R CHO CH_2OH CHO CH_2OH



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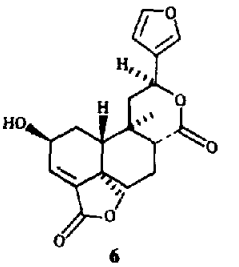

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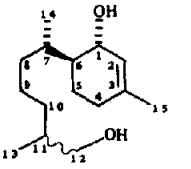

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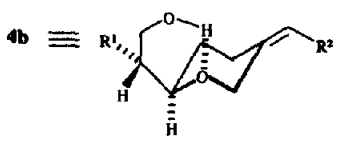

4b

species may show whether this is valid. As *Vittadinia* has generally been placed near *Aster* and *Erigeron* [14, 15] more results on the chemical constitution of these genera are also desirable.

EXPERIMENTAL

Plant material was collected in Sept. 1986 in SE Australia. The air-dried aerial parts were extracted with Et_2O–MeOH–petrol (1:1:1) and worked-up as reported previously [16]. The extract of 500 g *Vittadinia gracilis* gave by CC (silica gel) four fractions [1: petrol, 2: Et_2O–petrol (1:3), 3: Et_2O–petrol, (1:1) and Et_2O, 4: Et_2O–MeOH (9:1)]. The first fraction gave nothing of interest. TLC of fraction 2 gave 20 mg spathulenol, identical with an authentic sample (400 MHz ^{1}H NMR) and TLC of fraction 3 [Et_2O–petrol, (1:1)] afforded a mixt which gave by repeated HPLC [MeOH–H_2O (4:1) RP 8, *ca* 100 bar] 5 mg pure **4** (R_t 10.3 min), 40 mg of a mixt of **3** and **4** (*ca* 2:3) and 5 mg pure **3** (R_t 13.2 min). TLC of fraction 4 (Et_2O) gave three bands (4/1–4/3). HPLC of 4/1 [MeOH–H_2O, (4:1)] afforded 70 mg **2** (R_t 3.0 min), HPLC of 4/2 [MeOH–H_2O, (4:1)] 50 mg **1** (R_t 2.4 min) and 10 mg **5** (R_t 0.4 min) while HPLC of 4/3 [MeOH–H_2O, (7:3)] afforded 10 mg **6** (R_t 0.9 min). The extract of 400 g *V. cuneata* (voucher RMK 9600) gave by CC and TLC (Et_2O) 20 mg **7** (R_f 0.70).

18,19-*Dihydroxynerylgeraniol* (**1**). Colourless oil; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3600 (OH), 3030, 1635 (C=C); MS *m/z* (rel. int.): 286.230 [M − 2 H_2O]$^+$ (0.8) (calc. for $C_{20}H_{30}O$: 286.230), 255 (2.5), 187 (6.5), 175 (8), 93 (44), 69 (100). Acetylation(Ac_2O, 1 hr, 70°) afforded the triacetate **1Ac**, colourless oil; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1740, 1240 (OAc); MS *m/z* (rel. int.): 448.282 [M]$^+$ (0.3) (calc. for $C_{26}H_{40}O_6$: 448.282), 388 (1.5), 328 (5), 285 (8), 268 (12), 93 (61), 69 (100).

18-*Oxo*-19-*hydroxynerylgeraniol* (**2**). Colourless oil; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3600 (OH), 2720, 1680, 1640 (C=CCHO); MS *m/z* (rel. int.): 302.225 [M − H_2O]$^+$ (1.2) (calc. for $C_{20}H_{30}O_2$: 302.225), 284 (1), 269 (2), 69 (100). To 10 mg **2** in 1 ml MeOH 20 mg $NaBH_4$ were added. After 5 min at room temp. dil H_2SO_4 was added. Usual work-up gave after TLC 7 mg **1**, identical with the natural product.

Vittadinal (**3**). Colourless oil; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3605 (OH), 2720, 1725 (CHO), 1655 (C=C–); MS *m/z* (rel. int.): 302.225 [M − H_2O]$^+$ (2.3) (calc. $C_{20}H_{30}O_2$: 302.225), 273 (6), 234 (26), 109 (40), 93 (46), 82 (100), 69 (71); $[\alpha]_D \pm 0$. Reduction with $NaBH_4$ (as described above) afforded **3a**; colourless oil; MS *m/z* (rel. int.): 304.240 [M − H_2O]$^+$ (2.5) (calc. for $C_{20}H_{32}O_2$: 304.240), 273 (6), 93 (62), 82 (100), 69 (96).

Epi-*Vittadinal* (**4**). Colourless oil; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3600 (OH), 2720, 1725 (CHO), 1655 (C=C–); MS *m/z* (rel. int.): 302.255 [M − H_2O]$^+$ (2.8) (calc. for $C_{20}H_{30}O_2$: 302.225), 284 (1), 273 (3.7), 234 (25), 124 (27), 82 (100), 69 (73). Boranate reduction (as

described above) gave the diol **4a**; colourless oil; MS *m/z* (rel. int.): 304.240 $[M-H_2O]^+$ (3.8) (calc. for $C_{20}H_{32}O_2$: 304.240), 273 (4.7), 236 (21), 82 (100), 69 (86).

Vittagraciliolide (**5**). Colourless crystals, mp 221°, IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1770 (γ-lactone), 1660, 1340, 1120, 1095, 1010, 980, 935, 880; MS *m/z* (rel. int.): 356.126 $[M]^+$ (8) (calc. for $C_{20}H_{20}O_6$: 356.126), 326 (7), 312 (4), 282 (4), 202 (5), 94 (100); ^{13}C NMR ($CDCl_3$, C-1–C-20): δ 22.1 *t*, 27.3 *t*, 135.9 *d*, 136.8 *s*, 45.0 *s*, 31.0 *t*, 20.6 *t*, 48.1 *d*, 54.9 *s*, 45.4 *d*, 45.4 *t*, 76.5 *d*, 126.5 *s*, 108.3 *d*, 144.2 *d*, 139.7 *d*, 175.2 *s*, 168.0 *s*, 69.7 *t*, 107.3 *d*; $[\alpha]_D^{24}$ −144 ($CHCl_3$; *c* 0.07).

2β-Hydroxy-12-epi-bacchotricuneatin A (**6**). Colourless oil; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3600 (OH), 1770 (γ-lactone), 1720 (δ-lactone); MS *m/z* (rel. int.): 358.142 $[M]^+$ (3) (calc. for $C_{20}H_{22}O_6$: 358.142), 340 (2), 328 (4), 282 (2.5), 202 (6), 94 (100); $[\alpha]_D^{24}$ −65 ($CHCl_3$; *c* 0.97).

1,12-Dihydroxybisabol-2-ene (**7**). Colourless oil; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3600 (OH); MS *m/z* (rel. int.): 240.209 $[M]^+$ (3) (calc. for $C_{15}H_{28}O_2$: 240.209), 225 (9), 222 (21), 207 (6), 139 (28), 121 (31), 112 (28), 93 (52), 84 (100), 69 (44); ^1H NMR ($CDCl_3$): δ 4.02 (*br d*, H-1, J = 6 Hz), 5.38 (*br s*, H-2), 1.92 (*m*, H-4, H-7), 1.60 (*m*, H-4′, H-11), 1.36 (*m*, H-6), 3.49 and 3.43 (*dd*, H-12, J = 10.5, 5.5), 0.90 (*d*, H-13, J = 7), 0.79 (*d*, H-14, J = 7), 1.67 (*br s*, H-15); $[\alpha]_D^{24}$ +6 ($CHCl_3$; *c* 0.2).

Acknowledgement—We thank the Fonds der Chemischen Industrie, Frankfurt, for financial support.

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