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DITERPENES FROM *OLEARIA* SPECIES

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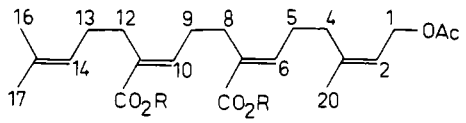
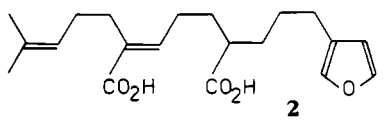
ABSTRACT.—The investigation of five *Olearia* species afforded, in addition to known compounds, 7α-acetoxybacchotricuneatin B [**3**], oleaxillaric acid [**1**], isolated as its dimethyl ester **1a**, and the aldehyde **6**, derived from thymol methyl ether. The structures were elucidated by high-field ^{1}H-nmr spectroscopy.

The large genus *Olearia* (Compositae, tribe Astereae, subtribe Asterinae) is distributed in Australia, New Zealand, New Guinea, and Lord Howe Island. Only a few species have been studied chemically. Clerodane derivatives were reported from two species (1,2), and flavones (1–3) and triterpenes (3,4) have been isolated. We have studied several further species and now report our findings.

The aerial parts of *Olearia axillaris* (DC.) F. Muell. ex Benth. afforded the dicarboxylic acid **1**, which was isolated as its dimethyl ester **1a**. The acid fraction did not show a methoxy signal in the ^{1}H-nmr spectrum, and the presence of a monomethyl



1 R=H **1a** R=Me



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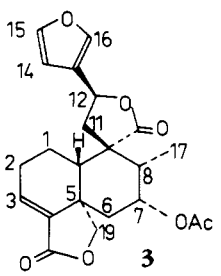

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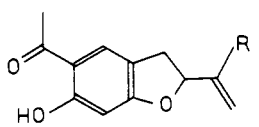
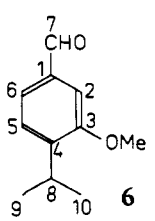


4 R=CH_2OH
5 R=CHO



6

ester could thus be excluded. The roots gave the aldehyde **5** (5), luteolin-8,3′-*O*-dimethyl ether, and the thymol derivative **6**.

The aerial parts of *Olearia brachyphylla* (F. Muell. ex Sonder) Wakef. gave tremetone, taraxasterol and its acetate, as well as sakuranetin; the roots gave squalene. The aerial parts of *Olearia lepidophyllum* (Pers.) Benth. afforded spathulenol and the furoditerpene **2** (6). The same diterpene also was present in the aerial parts of *Olearia muelleri* (Sonder) Benth., together with squalene and dammaradienol. The clerodane derivative isolated previously (2) could not be detected. Only the roots gave lupeyl acetate and squalene. Squalene, dammaradienol, and **2** were also isolated from the extract of the aerial parts of *Olearia pimeleoides* (DC.) Benth., together with the bacchotricuneatin derivative **3**. The roots gave squalene, coumaric acid, and the tremetone derivatives **4** (5) and **5** (5). The aerial parts of *Olearia subspicata* (Hook.) Benth. contain lupeol and its acetate was well as the furoditerpene **2**.

The ^{1}H-nmr spectrum of **1a** indicated the presence of an acetate and two carbomethoxy groups. In the ms the highest ion corresponds to $C_{22}H_{32}O_4$, which must be a fragment ion as no loss of HOAc could be detected from it. Thus, the molecular formula most likely was $C_{24}H_{36}O_6$. The ^{1}H-nmr spectrum showed four olefinic signals. This evidence, together with the molecular formula, suggested the presence of an alicyclic diterpene with three ester functions. The relative position of the various functions could be deduced from the ^{1}H-nmr spectrum. Irradiation at δ 5.10 sharpened two olefinic methyl signals. Accordingly, these signals were due to H-14, H-16, and H-17. A doublet at δ 4.58 required an acetoxy group at C-1. Irradiation of the latter signals collapsed the broadened triplet at δ 5.36 (H-2) to a singlet and sharpened the methyl singlet at δ 1.71. Accordingly, no carbomethoxy groups were at C-3 or C-15. Therefore, the carbomethoxy groups were at C-7 and C-11. The chemical shifts of the corresponding olefinic protons at C-6 and C-10 (δ 6.76 and 6.71) clearly indicated that they were β to a carbonyl group. Furthermore, the observed shifts required an *E* configuration as in the closely related furoditerpene **2** isolated from a *Microglossa* species (6). In the corresponding compounds with a *Z* configuration a chemical shift around 6.1–6.0 has been observed, for example in angelates (7). The configuration of the Δ^2 double bond followed from the shift of H-20 compared with the shift in a related diterpene of known configuration (8).

The structure of **3** followed from its ^{1}H-nmr spectrum (Table 1), which was very similar to that of bacchotricuneatin B (8). All signals were nearly identical except those of H-7, H-8, and H-17. Spin decoupling allowed the assignment of all signals. Irradia-

TABLE 1. ^{1}H-nmr Spectral Data of 7α-Acetobacchotricuneatin B [**3**] ($CDCl_3$, 400 MHz, δ values).[a]

H		H	
1α	1.49 dddd	11	2.57 dd
1β	2.02 br ddd	11′	2.47 dd
2α	2.30 m	12	5.39 dd
2β	2.52 m	14	6.39 br s
3	6.71 dd	15	7.44 t
6α	2.35 dd	16	7.46 br s
6β	1.55 ddd	17	1.09 d
7	5.34 ddd	19	5.30 d
8	1.95 dq	19′	3.87 dd
10	2.09 br d	OAc	2.13 s

[a]*J*(Hz): 1α,1β = 12.5; 1α,2α = 4.5; 1α,2β = 12.5; 1α,10 = 12.5; 1β,2α = 2; 1β,2β = 3; 2α,3 = 1.5; 2β,3 = 9; 6α,6β = 14.5; 6α,7 = 2; 5β,7 = 3.5; 6β,19′ = 2; 7,8 = 5; 8,17 = 7; 11,11′ = 14; 11,12 = 8; 11′,12 = 9; 14,15 = 1; 15,16 = 1; 19,19′ = 10.

tion of the methyl doublet at δ 1.09 collapsed the signal at δ 1.95 to a doublet. Irradiation of the latter collapsed the threefold doublet at δ 5.34 to a double doublet. Thus, the latter signal was due to H-7. The axial orientation was deduced from the observed couplings ($J_{6\alpha,7}=2, J_{6\beta,7}=3.5, J_{7,8}=5$) and inspection of a model; the couplings differed characteristically from those of the corresponding 7β-angeloyloxy derivative (9).

The molecular formula ($C_{11}H_{14}O_2$) and the ^{1}H-nmr spectrum of **6** indicated the presence of an aldehyde derived from thymol methyl ether. The relative position of the functions followed from the chemical shifts of the aromatic protons and from the presence of a small coupling between H-5 and H-8 that was visible by a sharpening of the H-5 doublet on irradiation of H-8.

The isolation of the diterpenes **1** and **2** may be of chemotaxonomic relevance as so far similar compounds have been reported from genera belonging to the same tribe (10–15). Also, clerodanes of type **3** are common in the Astereae.

EXPERIMENTAL

The air-dried plant material collected in southwest Australia (vouchers deposited in the U.S. National Herbarium) was extracted with a mixture of Et_2O-MeOH-petroleum ether (1:1:1), and the extracts were treated with MeOH to remove long-chain saturated hydrocarbons. The MeOH solutions were evaporated, and the residues were separated first by cc (Si gel, Et_2O/petroleum ether mixtures), then by tlc (Si gel PF 254), or finally by hplc (reversed-phase, RP 8 column, ca. 100 bar).

The aerial parts of *O. axillaris* (900 g, voucher RMK 9633B) gave, after reaction with CH_2N_2 of the Et_2O cc fraction by tlc (Et_2O), 30 mg **1a** (R_f 0.7). The roots (430 g) afforded 10 mg **6** (tlc: Et_2O-petroleum ether, 1:9, R_f 0.6), 8 mg **5**, and 2 mg luteolin-8,3′-*O*-dimethyl ether. The aerial parts of *O. brachyphylla* (370 g, voucher RMK 9604) gave 10 mg tremetone, 10 mg sakuranetin, 10 mg taraxasterol, and 10 mg of its acetate. The aerial parts of *O. lepidophylla* (600 g, voucher RMK 9603) afforded 15 mg spathulenol and 40 mg **2**, while the aerial parts of *O. muelleri* (680 g, voucher RMK 9609) gave 7 mg squalene, 5 mg dammaradienol, and 10 mg **2**. The roots gave 4 mg squalene and 10 mg lupeyl acetate. The aerial parts of *O. pimeleoides* (630 g, voucher RMK 9611) afforded 10 mg squalene and a mixture that gave by hplc (MeOH-H_2O, 3:2) 70 mg **3** (R_t 6.4 min) and 30 mg **2** (R_t 7.2 min). The roots (280 g) gave 20 mg squalene, 2 mg coumaric acid, 5 mg **4**, and 8 mg **5**. The aerial parts of *O. subspicata* (600 g, voucher RMK 9618) afforded 10 mg lupeol, 6 mg of its acetate, and 70 mg **2**.

DIMETHYL OLEAXILLARATE [**1a**].—Colorless oil; ir ν (CCl_4, cm^{-1}) 1740, 1240 (OAc), 1710 (C=CCO_2R); ms *m/z* $[M-HOAc]^+$ 360.230, (calcd. for $C_{22}H_{32}O_4$, 360.230) (1), $[M-MeOH]^+$ 328 (16), 296 (328 − MeOH) (7), 232 (15), 149 (40), 69 (C_5H_9) (199); ^{1}H nmr ($CDCl_3$) δ 4.58 (d, H-1), 5.36 (br t, H-2), 2.15 (br t, H-4), 2.29 (m, H-5, H-9, H-12), 6.76 (t, H-6), 2.41 (br t, H-8), 6.71 (br t, H-10), 2.05 (br dt, H-13), 5.10 (br t, H-14), 1.66 (br s, H-16), 1.57 (br s, H-17), 1.71 (br s, H-20), 2.04 (s, OAc), 3.73 and 3.71 (s, OMe) ($J_{1,2}=J_{4,5}=J_{5,6}=J_{8,9}=J_{9,10}=J_{12,13}=J_{13,14}=7$).

7α-ACETOXYBACCHOTRICUNEATIN B [**3**].—Colorless gum; ir ν (CCl_4, cm^{-1}) 1770 (γ-lactone), 1740 (OAc); ms *m/z* $[M]^+$ 400.152 (calcd. for $C_{22}H_{24}O_7$, 400.152) (0.7), $[M-CH_2O]^+$ 370 (38), 310 (370 − HOAc) (100). ^{1}H nmr see Table 1.

3-METHOXY-4-ISOPROPYL BENZALDEHYDE [**6**].—Colorless oil; ir ν (CCl_4, cm^{-1}) 1720 (CHO); ms *m/z* $[M]^+$ 178.099 (calcd. for $C_{11}H_{14}O_2$, 178.099) (48), $[M-Me]^+$ 163 (100), 135 (163 − CO) (11), 105 (26), 91 (17), 77 (14); ^{1}H nmr ($CDCl_3$) 7.35 (d, H-2), 7.37 (br d, H-5), 7.42 (dd, H-6), 9.93 (s, H-7), 3.38 (septet, H-8), 1.23 (d, H-9, H-10) ($J_{2,6}=2, J_{5,6}=8, J_{8,9}=J_{8,10}=7$).

LITERATURE CITED

1. J.T. Pinhey, R.F. Simpson, and I.L. Batey, *Aust. J. Chem.*, **24**, 2621 (1971).
2. P.R. Jeffries, J.R. Knox, K.R. Price, and B. Scaf, *Aust. J. Chem.*, **27**, 221 (1974).
3. H. Chivers, R.E. Corbett, and R.E.M. Mitchell, *J. Chem. Soc. C*, 1814 (1966).
4. R.C. Cambie and J.C. Parnell, *N.Z. J. Sci.*, 453 (1969).
5. F. Bohlmann and C. Zdero, *Phytochemistry*, **18**, 145 (1979).
6. A.A.L. Gunatilaka, B. Dhanabalasingham, L. Paredes, J. Jakupovic, F. Bohlmann, and N.K.B. Adikaram, *Phytochemistry*, **26**, 2408 (1987).
7. R.N. Barua, R.P. Sharma, G. Thyagarajan, W. Herz, and S.V. Govindan, *Phytochemistry*, **19**, 232 (1980).
8. F. Bohlmann, J. Jakupovic, and A. Schuster, *Phytochemistry*, **22**, 1637 (1983).

9. H. Wagner, R. Seitz, H. Lotter, and W. Herz, *J. Org. Chem.*, **43**, 3339 (1978).
10. F. Bohlmann, W. Kramp, M. Grenz, H. Robinson, and R.M. King, *Phytochemistry*, **20**, 1907 (1981).
11. F. Bohlmann and P.K. Mahanta, *Phytochemistry*, **18**, 1067 (1979).
12. J. Jakupovic, R.N. Baruah, F. Bohlmann, R.M. King, and H. Robinson, *Tetrahedron*, **41**, 4537 (1985).
13. F. Bohlmann, T.V. Chau-Thi, P. Singh, and J. Jakupovic, *Planta Med.*, 487 (1985).
14. F. Bohlmann and P. Wegner, *Phytochemistry*, **21**, 1693 (1982).
15. J. Jakupovic, S. Banerjee, F. Bohlmann, R.M. King, and H. Robinson, *Tetrahedron*, **42**, 1305 (1986).
16. F. Bohlmann, H. Robinson, and R.M. King, *Phytochemistry*, **19**, 2235 (1980).
17. F. Bohlmann, C. Zdero, R.M. King, and H. Robinson, *Phytochemistry*, **23**, 1979 (1984).

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