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PHENOLIC DITERPENOIDS OF *PODOCARPUS FERRUGINEUS* AND OTHER PODOCARPS*

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Key Word Index—*Podocarpus ferrugineus*; *Podocarpus* spp.; *Dacrycarpus vieillardii*; *Decussocarpus comptonii*; *Prumnopitys ferrugineus*; *Falcatifolium taxoides*; Podocarpaceae; phenolic diterpenoids; 19-hydroxyferruginol; 19-acetoxyferruginol; chemotaxonomy.

Abstract—19-Hydroxyferruginol and 19-acetoxyferruginol, two new naturally occurring phenolic diterpenoids, have been isolated from the heartwood of *Podocarpus ferrugineus*. Totarol and its derivatives have been obtained from *Podocarpus affinis*, *P. falcatus*, *P. koordersii*, *Dacrycarpus vieillardii* and *Decussocarpus comptonii* and podocarpic acid from *Falcatifolium taxoides*.

INTRODUCTION

Earlier we reported [1] the isolation of ferruginol (**1a**), sugiol (**1b**), and 5-dehydroferruginol from the heartwood of *Podocarpus ferrugineus* (natural habitat: New Zealand) and indicated the presence of traces of further diterpenoids. Two of the latter have now been identified as 19-hydroxyferruginol (**1c**) and its 19-acetate (**1d**).

RESULTS AND DISCUSSION

Rechromatography of phenolic fractions isolated from *P. ferrugineus* gave a gum which showed the same general features in the IR and ^{1}H NMR spectra as ferruginol. For example, a band at 865 cm^{-1} in the IR spectrum showed that the aromatic protons were not adjacent as they are in totaryl derivatives [2, 3] (ν_{max} cm^{-1}: 860–800). However, a doublet with bands of approximately equal intensity at 1380 and 1370 cm^{-1} in the IR spectrum of ferruginol was replaced by a single band at 1370 cm^{-1}. Also, in addition to a phenolic band at 1000 cm^{-1}, the spectrum of the gum showed a band at 1035 cm^{-1} indicative of a primary alcoholic group. If the hydroxy group was placed at C-4, its IR spectral frequency corresponded to an axial rather than an equatorial hydroxymethyl group [2]. This assignment was supported by the ^{1}H NMR spectrum which, in addition to showing peaks at δ 6.62 and 6.82 due to two isolated aromatic protons, showed a symmetrical doublet of doublets centred at 3.71 (J = 11 Hz) due to the protons of an axial hydroxymethyl group [4–6]. Their chemical shift and the presence of methyl peaks at δ 1.04 (H-18) and 1.13 (H-20), and a 6-proton *i*-propyl methyl doublet (J = 7 Hz) at 1.20 (H-16, H-17) indicated a 19-hydroxyferruginol structure as distinct from that of the recently isolated 16-hydroxyferruginol [7]. Since the ^{1}H NMR signal of an equatorial methyl group is shifted downfield in the presence of an axial hydroxymethyl group [5, 6], the downfield shift of the C-4 methyl group relative to that in ferruginol (δ 0.92) confirmed the stereochemistry at C-4. Acetylation of **1c** gave a diacetate (**1e**) whose IR (1750, 1730 cm^{-1}) and ^{1}H NMR (δ 2.16, 1.94) spectra showed the presence of aryl and alkyl acetate groups, respectively. An authentic sample of 19-hydroxyferruginol prepared from methyl 12-methoxypodocarpa-8,11,13-trien-19-oate (**2a**) [8] by established procedures [9–12] was identical IR, ^{1}H NMR, TLC) with the natural product.

Rechromatography of neutral fractions [1] gave a further gum which again showed similar spectral properties to those of ferruginol and 19-hydroxyferruginol. However, the IR spectrum showed a strong alkyl acetate band at 1730 cm^{-1} and an additional peak in the ^{1}H NMR spectrum at δ 2.00, and thus the compound was formulated as the 19-acetate (**1d**) of 19-hydroxyferruginol. This was confirmed when acetylation afforded the diacetate (**1e**).

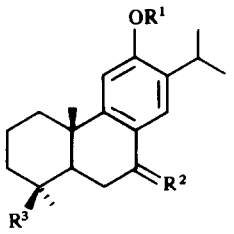
Examination of the woods of *Podocarpus affinis* (Fiji), *P. falcatus* (South Africa), *P. koordersii* (Java), *P. ustus* (New Caledonia), *Dacrycarpus vieillardii* (New Caledonia), *Decussocarpus comptonii* (New Caledonia), *Prumnopitys ferruginoides* (New Caledonia) and *Falcatifolium taxoides* (New Caledonia) gave results which are presented in Table 1. Of chemotaxonomic interest is the occurrence of totaryl derivatives in these and recently investigated species [13].

EXPERIMENTAL

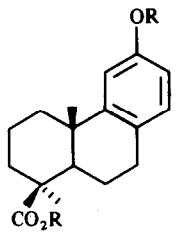
Mps are uncorr. UV: EtOH soln. IR: $CHCl_3$. ^{1}H NMR and ^{13}C NMR: $CDCl_3$ with TMS as internal reference (OH peaks exchanged with D_2O). MS were determined at 70 eV. Extraction of wood samples and work-up procedures were as described previously [13].

Podocarpus ferrugineus *G. Benn. ex D. Don.* The Et_2O eluates from the phenolic fractions from earlier work [1] were re-

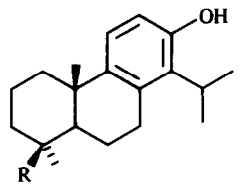
*Part LXVII in the series "Chemistry of the Podocarpaceae" For Part LXVI see Cambie, R. C., McNally, H. M., Robertson, J. D., Rutledge, P. S., and Woodgate, P. D., *Aust. J. Chem.* (in press).



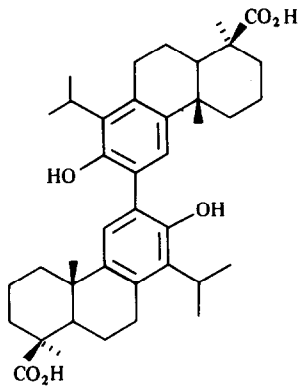
	R^1	R^2	R^3
1a	H	H_2	Me
1b	H	O	Me
1c	H	H_2	CH_2OH
1d	H	H_2	CH_2OAc
1e	Ac	H_2	CH_2OAc



	R
2a	Me
2b	H



	R
3a	Me
3b	CH_2OH
3c	CH=O
3d	CO_2H



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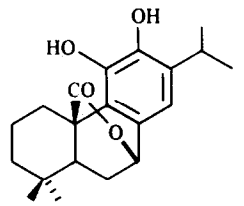

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chromatographed on activated Al_2O_3. Elution with C_6H_6–Et_2O (2:3) gave 19-hydroxyferruginol (**1c**) (see below) as a pale yellow gum (13 mg). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3600 (OH), 3340 br (OH), 2950, 2860, 1615, 1495, 1465, 1415, 1390, 1370, 1320, 1305, 1260, 1160, 1035, 1015, 1000, 965, 890, 865, 825; ^1H NMR: δ1.03 (*s*, H-18), 1.13, (*s*, H-20), 1.20 (*d*, J = 7 Hz, H-16, H-17), 2.82 (*m*, H-15), 3.71 (*dd*, J = 11 Hz, H-19), 5.66 (*s*, OH), 6.62 (*s*, H-11), 6.82 (*s*, H-14); diacetate (**1e**), oil. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1750, 1730; ^1H NMR: δ1.05 (*s*, H-18), 1.20 (*s*, H-20), 1.16 (*d*, J = 7 Hz, H-16, H-17), 2.06 (*s*, 19-OAc), 2.30 (*s*, 12-OAc), 4.15 (*dd*, J = 10 Hz), 6.84 (*s*, H-11), 6.95 (*s*, H-14).

The C_6H_6–Et_2O (1:1) eluates from the neutral fractions from earlier work [1] were rechromatographed on activated Al_2O_3. Elution with C_6H_6–Et_2O mixtures gave a pale yellow gum (10 mg). Prep. TLC gave 19-acetoxyferruginol (**1d**) as the major constituent. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 2950, 2920, 2860, 1730, 1620, 1500, 1460, 1410, 1380, 1365, 1325, 1310, 1260, 1160, 1120, 1090, 1020, 1000, 970, 890, 860; ^1H NMR (CCl_4): δ0.96 (*s*, H-18), 1.10 (*s*, H-20), 1.25 (*d*, J = 7 Hz, H-16, H-17), 2.00 (*s*, 19-OAc), 6.45 (*s*, H-11), 6.62 (*s*, H-14). Acetylation gave the diacetate (**1e**) (correct IR and TLC).

Partial synthesis of 19-*hydroxyferruginol.* Addition of methyl 13-acetyl-12-methoxypodocarpa-8,11,13-trien-19-oate [8] to MeMgI in Et_2O gave methyl 13α-hydroxyisopropyl-12-methoxypodocarpa-8,11,13-trien-19-oate, prisms (from petrol), mp 148–150° (lit. [9] 148–150°). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3450 br, 1725, 1620, 850; ^1H NMR: δ1.02 (*s*, H-18), 1.26 (*s*, H-20), 1.56 (*s*, H-16, H-17), 3.65 (*s*, OMe), 3.86 (*s*, OMe), 6.78 (*s*, H-11), 6.95 (*s*, H-14). Treatment with Ac_2O (reflux, 2 hr) gave methyl 13-isopropenyl-12-methoxypodocarpa-8,11,13-trien-19-oate, rods (from petrol), mp 120–121° (lit. [9] 120.5–121.5°). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1730, 1625, 1610, 1400, 855; ^1H NMR: δ1.05 (*s*, H-18), 1.26 (*s*, H-20), 2.08 (*s*, H-16), 3.68 (*s*, OMe), 3.78 (*s*, OMe), 5.06 (*s*, H-17), 6.75 (*s*, H-11), 6.85 (*s*, H-14). Hydrogenation over Adams' catalyst gave methyl 13-isopropyl-12-methoxypodocarpa-8,11,13-trien-19-oate, mp 110° (lit. [9] 109–109.5°). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1720, 1625, 1610, 1575, 1400, 840. Reduction with $LiAlH_4$ gave methyl 13-isopropyl-12-methoxypodocarpa-8,11,13-trien-19-ol, needles (from petrol), mp 83–85° (lit. [11] 83–85°). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3640, 3440 br, 1615, 1575, 850; ^1H NMR: δ1.03 (*s*, H-18), 1.18 (*s*, H-20), 1.17 (*d*, J = 7 Hz, H-16, H-17), 3.69 (*dd*, J = 11 Hz, H-19), 3.71 (*s*, OMe), 6.72 (*s*, H-11), 6.84 (*s*, H-14). Demethylation with BBr_3 in CH_2Cl_2 gave 19-hydroxyferruginol (**1c**), plates (from petrol–$CHCl_3$), mp 180–186° (lit. [12] 185.4–186.4°) (Found: C, 79.5; H, 10.3. Calc. for $C_{20}H_{30}O_2$: C, 79.4; H, 10.0%). The IR and ^1H NMR spectra were identical with those of the natural product. ^{13}C NMR: δ19.0 (*t*, C-2), 19.4 (*t*, C-6), 22.6, 22.7 (2*q*, C-16, 17), 25.7 (*q*, C-18), 26.7 (*d*, C-15), 26.7 (*q*, C-20), 30.3 (*t*, C-7), 35.1 (*s*, C-4), 37.4 (*s*, C-10), 38.6 (*t*, C-1), 38.9 (*t*, C-3), 51.2 (*d*, C-5), 65.2 (*t*, C-19), 111.0 (*d*, C-11), 126.5 (*s*, C-8), 126.5 (*d*, C-14), 131.9 (*s*, C-13), 147.9 (*s*, C-9), 151.0 (*s*, C-12). Diacetate (**1e**), ^{13}C NMR: δ18.9 (*t*, C-2), 19.2 (*t*, C-6), 21.0 (*q*, COMe), 21.0 (*q*, C-17), 22.9 (*q*, C-16), 25.6 (*q*, C-18), 26.8 (*d*, C-15), 27.2 (*q*, COMe), 27.3 (*q*, C-20), 30.5 (*t*, C-7), 35.9 (*s*, C-4), 37.1 (*t*, C-1), 37.5 (*s*, C-10), 38.7 (*t*, C-3), 50.9 (*d*, C-5), 66.9 (*t*, C-19),

Table 1. Wood extractives of podocarps

Compound	*Podocarpus affinis*	*Podocarpus falcatus*	*Podocarpus koordersii*	*Podocarpus ustus*	*Dacrycarpus vieillardii*	*Decussocarpus comptonii*	*Prumnopitys ferruginoides*	*Falcatifolium taxoides*
Totarol (**3a**)	+	+	+	−	+	+	−	−
19-Hydroxytotarol (**3b**)	+	−	−	−	+	+	−	−
19-Oxototarol (**3c**)	−	−	−	−	+	−	−	−
4β-Carboxy-19-nortotarol (**3d**)	+	+	+	−	−	−	−	−
Macrophyllic acid (**4**)	−	+	+	−	−	−	−	−
Carnosol (**5**)	−	−	+*	−	−	−	−	−
Podocarpic acid (**2b**)	−	−	−	−	−	−	−	+
Sitosterol	−	−	−	+	+	−	+	+

*Tentative identification.

118.1 (*d*, C-11), 126.9 (*d*, C-14), 132.6 (*s*, C-8), 136.9 (*s*, C-13), 146.2 (*s*, C-9), 148.0 (*s*, C-12), 169.9 (*s*, CO), 171.4 (*s*, CO).

Podocarpus affinis *Seem.* The wood (160 g) gave an EtOAc extract (1.0 g) which was separated into a neutral fraction (0.3 g) and an acid fraction (0.7 g). Prep. TLC (C_6H_6) of the neutral fraction gave totarol (**3a**) (*ca* 2 mg), mp and mmp 126–128° (correct UV, IR, and MS), and 19-hydroxytotarol (**3b**) (*ca* 1 mg) (correct UV, IR, and MS). Prep. TLC of the acid fraction gave 4β-carboxy-19-nortotarol (**3d**) (*ca* 3 mg) (correct UV, IR, and MS) purified as the acetate, mp and mmp 230–235° (correct UV and IR).

Podocarpus falcatus *(Thunb.) de Laub.* The wood (153 g) gave an Et_2O extract (0.47 g) which was separated into a neutral fraction (0.3 g) and an acidic fraction (0.44 g). Prep. TLC (C_6H_6) of the neutral fraction gave totarol (**3a**) (5 mg), mp and mmp 126–127° (correct UV and IR). Prep. TLC (Et_2O–C_6H_6, 2:1) of the acid fraction gave macrophyllic acid (**4**) (*ca* 1 mg), mp 230–235° (correct UV and IR), and 4β-carboxy-19-nortotarol (**3d**) as a gum (5 mg) (correct UV and IR), which was purified as the acetate, mp and mmp 238–245° (correct UV and IR).

Podocarpus koordersii *Pilger.* The wood (273 g) gave an Et_2O extract (1.4 g) which was separated into a neutral fraction (0.42 g) and an acid fraction (0.25 g). Prep. TLC (C_6H_6) of the neutral fraction gave totarol (**3a**) (*ca* 1 mg) (correct UV, IR, and MS). Prep. TLC (Et_2O–C_6H_6, 2:1) of the acid fraction gave: (i) macrophyllic acid (**4**) (*ca* 2 mg), mp and mmp 230–240° (correct UV and IR); (ii) impure carnosol (**5**) [14] (*ca* 1 mg), mp 150–200°, UV λ_{max} nm: 285; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3500 sh (OH), 3400–3200 br (OH), 1740 (CO), 1690, 1590; MS *m/z* (rel. int.): 330 $[M]^+$ (30), 315 $[M-Me]^+$ (28), 284 (50), 269 (55), 251 (20), 241 (30), 227 (32), 213 (68), 176 (100), 151 (30). Oxidation with bromine water gave a product with UV λ_{max} nm: 425; (iii) 4β-carboxy-19-nortotarol (**3d**) (5 mg) (correct UV and IR) purified as the acetate, mp and mmp 235–239° (correct UV and IR).

Podocarpus ustus *Brongn. & Gris.* The wood (58 g) gave an Et_2O extract (0.27 g) which was chromatographed on Al_2O_3. Elution with hexane–Et_2O containing increasing amounts of Et_2O gave sitosterol (*ca* 5 mg) (correct IR and TLC).

Dacrycarpus vieillardii *(Parl.) de Laub.* The wood (75 g) gave a hexane extract (0.54 g) and an Et_2O extract (0.28 g) which were combined and chromatographed on Al_2O_3. Elution with hexane–Et_2O mixtures gave successively totarol (**3a**), 19-hydroxytotarol (**3b**), 19-oxototarol (**3c**) (each *ca* 1–3 mg), and sitosterol (8 mg), each identified by UV, IR, and TLC comparison with authentic samples.

Decussocarpus comptonii *(Buchholz) de Laub.* The wood (69 g) gave a hexane extract (0.41 g) and an Et_2O extract (0.51 g) which were combined and chromatographed on Al_2O_3. Elution with hexane–Et_2O gave totarol (**3a**) and 19-hydroxytotarol (**3b**), each (*ca* 2–3 mg) identified by UV, IR, and TLC comparison with authentic samples.

Prumnopitys ferruginoides *(Compt.) de Laub.* The wood (54 g) gave an Et_2O extract (0.60 g) which was chromatographed on Al_2O_3. Elution with hexane–Et_2O mixtures gave sitosterol (*ca* 5 mg) (correct IR and TLC).

Falcatifolium taxoides *(Brong. & Gris.) de Laug. (syn.* Dacrydium taxoides). The wood (60 g) gave a hexane extract (0.43 g) and an Et_2O extract (20 mg) which were combined and chromatographed on Al_2O_3. Elution with hexane–Et_2O and Et_2O–EtOAc mixtures gave sitosterol (*ca* 5 mg) (correct IR, MS, and TLC) and then podocarpic acid (**2b**) (*ca* 5 mg) (correct UV and IR); methyl ester (**2a**), mp and mmp 198–200° (correct IR).

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