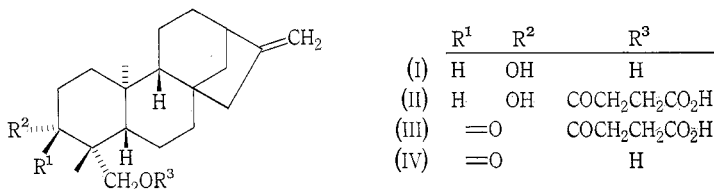


SUBSTANCES DERIVED FROM *GOODENIA STROPHIOLATA* F. MUELL.*

By E. J. MIDDLETON† and P. R. JEFFERIES†

As part of our work on plants from the drier areas of Western Australia we have examined *Goodenia strophiolata* F. Muell. (Goodeniaceae). This plant is a glabrous viscid erect shrub growing to about 4 ft and is common in the lower rainfall areas of southern and south-eastern parts of Western Australia. Apart from one species *Goodenia* appears to be endemic to Australia¹ and about half (c. 60) of the species are peculiar to Western Australia. As a rule, they are small shrubs or herbs and are common in the Eremean zone. Prior work on the genus is limited to the isolation of ursolic acid² from *G. ovulata* and an indication for malvidin in *G. paniculata*.³



Extraction of *G. strophiolata* with ether and fractionation gave ursolic acid, isolated as the methyl ester acetate, (–)-kaur-16-ene-3 α ,19-diol (I), the succinate (II) of the diol, and 5,7,3',4'-tetrahydroxy-3-methoxyflavone. The latter occurs as a glycoside⁴ in *Stizolophus balsamita* and has been suggested as a constituent of the flowers of *Nicotiana tabacum*.⁵ We had encountered the kaurenediol (I) before in *Beyeria leschenaultii*⁶ and *B. latifolia*⁷ and it has recently been obtained from *Helichrysum dendroideum*.⁸ *G. strophiolata* is the preferred source since the diol and its esters represent c. 3.3% of the dry plant. The structure of the succinate follows from its hydrolysis to the diol (I) and succinic acid, and by its oxidation to the ketone (III). The latter was hydrolysed to the ketol (IV) by potassium carbonate solution.

* Manuscript received April 16, 1968.

† Department of Organic Chemistry, University of Western Australia, Nedlands, W.A. 6009.

¹ Burbidge, N. T., "Dictionary of Australian Plant Genera, Gymnosperms and Angiosperms," p. 137. (Angus & Robertson: Sydney 1963.)

² Lahey, F. N., and Strasser, P. H. A., *J. Proc. Aust. chem. Inst.*, 1947, **14**, 432.

³ Gascoigne, R. M., Ritchie, E., and White, D. E., *J. Proc. R. Soc. N.S.W.*, 1948, **82**, 44.

⁴ Utkin, L. M., and Serebryakova, A. P., *J. gen. Chem. USSR*, 1964, **34**, 3539.

⁵ Yang, C. H., Braymer, H. D., Murphy, E. L., Chorney, W., Scully, W., and Wender, S. H., *J. org. Chem.*, 1960, **25**, 2063.

⁶ Baddeley, G. V., Jefferies, P. R., and Retallack, R. W., *Tetrahedron*, 1964, **20**, 1983.

⁷ Jefferies, P. R., and Retallack, R. W., *Aust. J. Chem.*, 1968, **21**, 2085.

⁸ Lloyd, H. A., and Fales, H. M., *Tetrahedron Lett.* 1967, 4891.

Experimental

For general details see ref.⁹

Extraction

Dried milled plant (6.9 kg) collected 42 miles east of Norseman, W.A., during October 1963 was extracted with ether and the extract washed with aqueous 8% NaHCO₃, then 5% NaOH solution. Insoluble salts which precipitated during the latter wash were filtered off. Isolation of the acids from the bicarbonate wash with ether gave a viscous residue which partly crystallized. The acid (II) (144 g) was obtained by filtration and washing the precipitate with a little ether, then concentrating the filtrate for further crystallization and repeating the process several times. Recrystallization from benzene, then aqueous methanol (charcoal) gave needles of 19-(3-carboxypropionyloxy)-(-)-kaur-16-ene-3 α ,19-diol (II), m.p. 155–157°, [α]_D -62.5° (c, 1.13) (Found: C, 71.2; H, 9.0; O, 19.9. C₂₄H₃₆O₅ requires C, 71.25; H, 9.0; O, 19.8%). ν_{\max} (Nujol mull) 3500, 3200, 3070, 1690, 1645, 1200, 880 cm⁻¹. ν_{\max} (CS₂) 3600, 3480, 3070, 1730, 1700 cm⁻¹. The n.m.r. spectrum (pyridine) had peaks at 1.05, 1.37 (C 4-Me, C 10-Me), 2.05 (C 15-H₂), 2.58 (C 13-H), 2.87 (succinate), 3.48 (*W*₁ 16 c/s; C 3 β -H), 4.62, 4.68 δ (C 19-H₂, *J* 11.5 c/s).

A sample of the residue from the bicarbonate extract (10 g) was chromatographed on silicic acid (250 g) and elution with light petroleum-ether (4 : 1) gave an oil whose n.m.r. spectrum showed that it was essentially the 3-acetate of the succinate (II). The remainder of the residues was hydrolysed by refluxing with 5% potassium hydroxide in 90% ethanol for 2 hr, and then water was added to the hot mixture until crystallization commenced. In this way (-)-kaur-16-ene-3 α ,19-diol (I) (60 g) separated. A further crop (16 g) was obtained by similar hydrolysis of the neutral residues (70 g) from the plant extract. The analytical sample was crystallized from benzene-light petroleum as needles, m.p. and mixed m.p. 184–185°, [α]_D -73° (c, 1.57) (Found: C, 78.9; H, 10.4. C₂₀H₃₂O₃ requires C, 78.9; H, 10.6%). The diacetate had m.p. and mixed m.p. 114–115°.⁶

The material (90 g) recovered from the 5% NaOH wash of the plant extract was re-partitioned with 8% NaHCO₃ (discarded), 5% Na₂CO₃, and 5% NaOH. A concentrated ether solution of the sodium carbonate extract (45 g) slowly deposited yellow needles (13.7 g). Crystallization from ethanol-benzene yielded yellow needles of 5,7,3',4'-tetrahydroxy-3-methoxyflavone, m.p. 275–278° (lit.¹⁰ 273–275°) (Found: C, 60.6; H, 4.0; OMe, 9.95. C₁₆H₁₂O₇ requires C, 60.8; H, 3.8; 1 \times OMe, 9.8%).

The tetraacetate, prepared using HClO₄ catalyst, had m.p. 180–182° (lit.¹⁰ 182–184°). Methylation with Me₂SO₄-K₂CO₃ gave quercetin pentamethyl ether, m.p. and mixed m.p. 152–153°. 5,7,3',4'-Tetraethoxy-3-methoxyflavone, prepared similarly with Et₂SO₄-K₂CO₃, had m.p. 149–150° alone or mixed with a sample prepared from rutin.¹¹

The insoluble salts were suspended in ether and acidified with dilute hydrochloric acid. The insoluble material (17 g) was filtered off and a portion (3.0 g) methylated with ethereal diazomethane. The product was acetylated with acetic anhydride and pyridine at room temperature. Crystallization of the product from ethanol gave methyl ursolate acetate, m.p. and mixed m.p. 245–247° (lit.¹² 246–247°) (cap.), [α]_D +66° (c, 1.72) (Found: C, 77.7; H, 10.2. C₃₃H₅₂O₄ requires C, 77.3; H, 10.2%). Saponification with 5% potassium hydroxide in refluxing methanol gave methyl ursolate, m.p. and mixed m.p. 168–170°.

Hydrolysis of 19-(3-Carboxypropionyloxy)-(-)-kaur-16-ene (II)

The hydroxy succinate (II) (3.34 g) was dissolved in a mixture of potassium hydroxide (11 g), ethanol (75 ml), and water (50 ml) and refluxed for 2 hr. The alcohol was distilled and the

⁹ Henrick, C. A., and Jefferies, P. R., *Tetrahedron*, 1965, **21**, 3219.

¹⁰ Kuhn, R., and Löw, I., *Ber. dt. chem. Ges.*, 1944, **77**, 211.

¹¹ Anand, N. K., Gupta, S. R., Jain, A. C., Mathur, S. K., Pankajamani, K. S., and Seshadri, T. R., *J. scient. ind. Res. B*, 1962, **21**, 322 (*Chem. Abstr.*, 1962, **57**, 13712).

¹² Elsevier's "Encyclopedia of Organic Chemistry." Vol. 14, p. 526. (Elsevier: Amsterdam 1940.)

neutral product filtered (2.64 g) and recrystallized from benzene-light petroleum to give (–)-kaur-16-ene-3 α ,19-diol (I) as needles, m.p. and mixed m.p. 184–185°. The filtrate was concentrated, acidified, and continuously extracted with ether. The extract was evaporated and the residue (2.09 g) re-extracted with dry ether to give succinic acid (780 mg), m.p. and mixed m.p. 183–185°. The acid was treated with thionyl chloride to give succinic anhydride, m.p. and mixed m.p. 119–121°. The anhydride, with aniline in benzene gave succinilic acid, m.p. and mixed m.p. 151–153°.

19-(3-Carboxypropionyloxy)-(–)-kaur-16-ene-3-one (III)

The hydroxy succinate (II) (1.08 g) in acetone (25 ml) was oxidized with Jones reagent (0.73 ml; 2.1 equiv.) at 0° for 5 min. Isolation of the product with ether and crystallization from light petroleum-benzene gave the *ketone* (III) as needles, m.p. 132–133°, $[\alpha]_D -42^\circ$ (c, 1.82) (Found: C, 71.8; H, 8.7. $C_{24}H_{34}O_5$ requires C, 71.6; H, 8.5%). Absorption in the i.r. occurred at 3350–3100 and 1690 (CO_2H), 1750 (CO_2R), 1710 (cyclohexanone), 880 cm^{-1} ($=CH_2$). The n.m.r. spectrum had peaks at 1.15, 1.24 (C10–Me, C4–Me), 2.08 (C15– H_2), 2.61 (5H; C13–H, succinate); 4.02, 4.55 (AB, J 11 c/s; C19– H_2) and 4.78 δ (C17– H_2).

19-Hydroxy-(–)-kaur-16-en-3-one (IV)

The keto succinate (III) (0.7 g) was dissolved in water (100 ml) containing K_2CO_3 (5 g) and KCl (10 g), and the solution continuously extracted with ether for 3 days. The ether extract was evaporated and the residue crystallized from aqueous methanol and then light petroleum as dimorphic prisms (0.38 g) of the *ketol* (IV), m.p. 110–111° and 116–117°, $[\alpha]_D -137^\circ$ (c, 0.54) (Found: C, 79.5; H, 10.3. $C_{20}H_{30}O_4$ requires C, 79.4; H, 10.0%). The i.r. spectrum (0.003M in CCl_4) had ν_{max} 3500 (bonded OH), 3070, 875 ($C=CH_2$), and 1690 cm^{-1} (bonded ketone). The n.m.r. spectrum (CCl_4) had peaks at 0.91, 1.00 (C10–Me, C4–Me); 3.16, 3.60, (AB, J 11.5 c/s); 4.55 δ (C17– H_2).

Acknowledgment

We thank the Botany Branch of the State Agriculture Department for taxonomic information.